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JEFFERSON AND PENNSYLVANIA HOSPITALS

AORTITIS[1]

The Common Neglect of Examination of the Aorta for Disease Other than Aneurysm. Aortitis Due to Infectious Diseases. Syphilitic Aortitis. Aortitis and Rheumatic Fever. Illustrative Case Reports. Clinical Features. Diagnosis. Treatment.

ONE of the curious points in regard to aortitis is the slight attention that has been paid to it in American medical literature until comparatively recently. What explanation is to be given for this is a difficult question. Aneurysm has not failed to have sufficient notice, but this more common aortic change has been almost entirely neglected. The heart is examined as a matter of routine, but too often no care is taken to investigate the condition of the aorta. If you will do this systematically as part of the routine examination you will be surprised to find how much information you can obtain in a very short time by the ordinary methods of examination. In some cases an *x*-ray examination is required to make the diagnosis definite, but this is the exception. Your eyes and hands are usually all that you require, with, of course, some brains behind them.

Much of the discussion on the subject of chronic aortitis is bound up with the larger question of arteriosclerosis, but I hope

[1] This report is a combination of several clinics given at the Jefferson and Pennsylvania Hospitals.

to show you that there are other relations which are of importance. I have said to you that we cannot hope to carry in our minds a complete store of knowledge about every subject, and it is therefore important to know where to go when we wish more information. Let me suggest to you a storehouse of knowledge relating to arteriosclerosis and aortitis—the work by Sir Clifford Allbutt. For the answer to any question connected with these subjects and angina pectoris do not fail to consult these volumes.

You must have been impressed in the autopsy room by the appearance of the aorta in many of the subjects. Its inner surface often shows scars and marked irregularities, here an elevation and there a depression, with perhaps some calcareous areas, so that you may have wondered how the wall withstood the constant pressure of the blood. Sometimes, as you know, it does not, and aneurysm results. Let us discuss some of the conditions which lead to these changes. It aids our conceptions of the process if we can trace the course of events. Anatomically, there are some points worthy of notice. We cannot dissociate the consideration of the aorta from the aortic orifice and valves —disease of one often means disease of the other. In rheumatic fever and syphilis this is particularly common. Nor must we forget that the orifices of the coronary arteries are situated close to the valves and naturally may suffer in disease of the first part of the aorta. This damage we often have to infer rather than prove, but it is evident that it must play an important part in prognosis.

What are the causes of injury to this region? It is evident that the aorta may suffer in common with the arteries generally, but your observation of autopsies must have impressed you with the curious irregularity of lesions of the arterial system. We find in some cases that the damage in the aorta may be local, and involve only the arch or extend as far as the point where the aorta passes through the diaphragm and stop abruptly there. Let us discuss some of the causes of aortitis, and in this we have to recognize the large part played by infections. It is interesting to look back over a period of twenty years and observe how the

importance given to the effect of infectious diseases on the arterial system has steadily increased. They are now recognized to play a much more important part than was formerly thought.

AORTITIS DUE TO INFECTIOUS DISEASES

It is probable that any infectious disease may cause aortitis, but two stand out as particularly frequent—rheumatic fever and syphilis—and to these we shall give special attention. It would be of interest to know the relative frequency with which aortitis accompanies and follows the various infections, but I know of no statistics which give us exact information. It should be possible in a carefully studied series of cases of rheumatic fever to determine this point. My opinion is that the tendency has been to give too little place to this disease, and in some quarters syphilis is regarded as practically the only causal infection. This is certainly not correct. In a series of 60 cases of dilatation of the aorta, which may be regarded as chronic aortitis, about one-third gave a history of rheumatic fever. What was particularly striking were the figures in the patients below the age of forty years; of these one-half had suffered from rheumatic fever. In this series syphilis could not be proved in more than one-half of the cases. It is wise always to have syphilis in mind, as was demonstrated by one patient whom I have observed for years. He had a marked chronic aortitis, but gave no history of syphilis, showed no signs of it, and the blood Wassermann reaction was negative on several occasions. Some years later he showed some obscure symptoms of disease of the nervous system. The spinal fluid gave a positive Wassermann and globulin reaction and showed an increase of cells. This leads to the belief that doubtless the aortic condition was due to syphilis, but this would not have been proved but for the nervous system involvement.

1. **Syphilitic Aortitis.**—Syphilis must be regarded as the great cause of aortitis, and it is well to keep it in mind in every case of syphilis and to consider syphilis in every case of aortitis. This patient demonstrates some of the most marked features.

CASE I.—The patient is a colored female, single, aged eighteen, admitted on January 25, 1917, who comes complaining of pain in the chest and some shortness of breath.

The family history is negative.

Personal History.—Other than measles and whooping-cough in childhood, she has not had any acute disease. There is no history of rheumatic fever. She has not suffered from throat trouble and has not had any cough or shortness of breath before the present illness. She had suffered somewhat from leukorrhea for a couple of years, but there is nothing in the history to suggest definitely a gonococcus infection. There is no history of any luetic infection. She has suffered somewhat from menstrual irregularity.

Present Illness.—It is not easy to obtain a definite statement from her as to the exact time of onset, but evidently for about four months she has been troubled by thoracic pain which has become distinctly worse recently. When asked to show the seat of pain, she refers it to the upper part of the sternum, and, in addition, states that she has suffered from pain which she refers to the region of the heart, pointing to the area inside and a little below the nipple. This latter she states has not been as severe as the pain higher up in the chest. In the last two months she has had a certain amount of cough and has noted at times that her voice was very husky. During a considerable part of her illness she has been in bed, the reason for this being that exertion made the pain worse and caused shortness of breath.

Examination.—The patient is well nourished, does not show exophthalmos, but the pupils are slightly unequal, the left being a little the larger. The thyroid is just palpable. There is slight general glandular enlargement. The thoracic expansion is distinctly less in the upper left chest and there is slight dulness on percussion in front and more marked dulness in the upper left back. The breath sounds generally are very feeble, and this is most marked over the area of dulness in the upper left thorax. Vocal fremitus is very slightly present everywhere. The patient's voice is feeble and, while slightly husky, cannot be said to have a brassy quality.

Heart: There is no precordial bulging, but you can see the very wide-spread diffuse fluttering cardiac impulse. The apex-beat is not definitely made out, but there is a fairly marked impulse in the fifth interspace about 8 cm. from the midline. There is a slight systolic shock, but no thrill. There is a well-marked visible impulse in the second right interspace and first and second left interspaces. No thrill is felt at the base. Of special interest is the result of percussion over the manubrium and adjoining interspaces. In the first interspace dulness extends $3\frac{3}{4}$ cm. to the right and 5 cm. to the left; in the second interspace, 3 cm. to the right and $4\frac{1}{2}$ cm. to the left; and in the fourth interspace, $3\frac{1}{2}$ cm. to the right and 9 cm. to the left. At the apex both sounds are heard, the first being sharp and short; there is no definite murmur. Just inside the apex there is a perfectly distinct soft systolic murmur. In the tricupsid area the sounds are feeble and there is a soft systolic murmur. From the third interspace, on both sides of the sternum up to the clavicles, there is a systolic murmur which is very intense on the right and much louder and rougher on the left, with the maximum in the second left interspace. It is well heard over the upper sternum. There is no diastolic murmur. The pulse is 120, of small volume, not collapsing, and it seems equal in the two radials. The systolic pressure is 108. There is a very marked visible pulsation in the neck, especially in the suprasternal notch. The aorta can be felt behind the upper end of the sternum.

The blood on admission showed Hb., 20 per cent.; reds, 2,010,000; leukocytes, 10,000; the differential count is normal. There is a strongly positive Wassermann reaction. On February 9th the count showed Hb., 33 per cent.; reds, 3,420,000; leukocytes, 12,800. The urine is practically clear. The patient has markedly irregular fever, averaging about 100° F., occasionally going up to 102° F. and even to 104° F. (Fig. 15). The pulse-rate has been rapid, at first between 100 and 120, and occasionally rising to 130 to 140. The *x*-ray plate showed considerable enlargement of the aorta, but no sign of aneurysm.

We have the problem of a young woman complaining of thoracic pain, showing signs of an infection, as shown by the

fever curve, with a rapid, feeble heart, but no definite signs of endocarditis, and positive evidence of marked enlargement of the aorta. A number of explanatory diagnoses may occur to you, but the combination of pain referred to the upper sternum with signs of enlargement of the aorta is very suggestive of acute aortitis, and the results of the *x*-ray study confirm this. The result of the Wassermann reaction is strongly positive, which strengthens the diagnosis. The evidence of disease in the heart muscle is to be explained as due to syphilitic myocarditis. Pain referred to the precordium is an important sign of this. Some de-

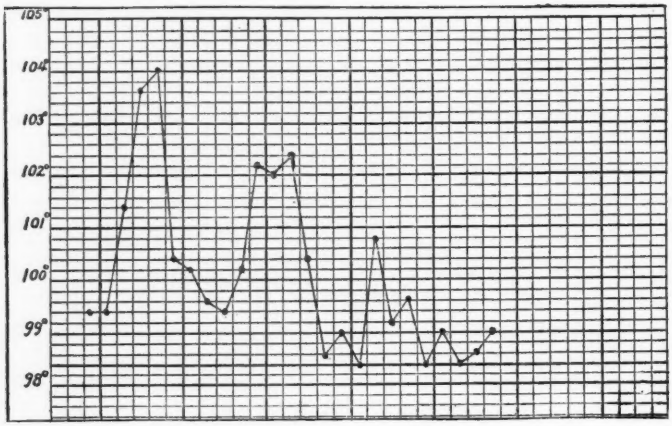

Fig. 15.—Temperature record in a case of syphilitic aortitis.

pendence will be placed on the result of the therapeutic test, the results of which are to be reported later. There is a marked secondary anemia, and this, in all probability, plays a part in the myocardial disturbance.

You may ask what therapy is best to employ. Should we give salvarsan or neosalvarsan? If so, it should be done very cautiously and in small doses. My preference at first is to give salvarsan in small doses (0.2 gm.) at intervals of about a week, and to use mercury by inunction and iodid by mouth, both in good doses, a dram of mercurial ointment each day by inunction,

and iodid in doses of 30 gr. a day, gradually increased to 90 gr. a day.

Under this treatment she improved rapidly, and by February 22d the pain had disappeared, the temperature had fallen to normal rather rapidly, but the dulness over the manubrium and adjoining interspaces was practically the same with well-marked pulsation in the second right interspace, which could not be definitely felt. The aorta was still palpable in the suprasternal notch. The systolic murmur at the base, which had been so loud, had become much less, and was practically not heard at all to the right of the sternum. The pulse-rate has fallen to between 70 and 80 and the systolic pressure has risen to 120. The cardiac dulness has decreased, the visible impulse is less diffuse, and she has a fairly marked apex-beat, all suggesting improvement in the myocardial condition. The anemia is also much less. Three months later she reported herself as very well.

In this patient the question arises as to whether the infection was congenital or acquired. It may be either, but as she shows no other evidence of congenital syphilis, the chances are that it was acquired.

As regards the occurrence of syphilis in the aorta, we know that this is a favorite place for the spirochetes to settle and remain; in fact, it is a question whether having once penetrated there and become well established, they ever disappear. In this connection the work of Warthin is important. One is impressed by the number of cases in which he found spirochetes in the tissues even in patients never suspected of having had syphilis. As a matter of historic interest attention should be drawn to the work of Hodgson, who described many of the features of chronic aortitis. His work seems to be little known, and has been appreciated more by French writers than by workers in Britain or America. The French often refer to the combination of dilatation of the aorta with aortic insufficiency as "maladie de Hodgson." To Francis H. Welch is due much credit for emphasizing the importance of syphilis in lesions of the aorta. I give his name in full, as some writers have confused him with W. H. Welch, of Baltimore.

One problem of great importance is the explanation for the special distribution of syphilis in the aorta. The ascending and transverse portions of the arch are particularly susceptible. In addition, in the abdominal aorta the point about which the celiac axis comes off is apparently also particularly liable to be involved. It has been supposed that this was largely influenced by the infection being carried by the vasa vasorum, but if this was the case we do not have an explanation for the localization above mentioned. The explanation given by Dr. Klotz is that the relationship of the lymphatics probably gives the key. The first portion of the aorta shows a very much greater number of lymph-channels than elsewhere. The lymphatics in the aorta follow the course of the vasa vasorum, and this probably accounts for the perivascular infiltration which is so prominent in syphilitic aortitis. This distribution of syphilis by the lymphatics is apparently exactly comparable to what may take place in lobar pneumonia. In general, when infection localizes in the aorta it seems to begin in the outermost layers and gradually extends to the media.

Symptoms.—In connection with the question of syphilitic aortitis we have to remember the division into acute and chronic forms. The case given before is an example of the former; the features of the chronic form do not differ materially from those of chronic aortitis in general. At present we are discussing the acute aortitis. The interval between the time of infection and the manifestation of aortitis varies within wide limits. In some cases the interval is comparatively short, less than a year; as to a longer interval, it is difficult to set limits. In the majority of the cases which I have seen it has been from two to five years. In the present case we have no definite information as to the interval. It is well to remember that the infection may have been before birth, but she shows no signs of congenital lues. Some of the clinical features may be discussed in detail.

General Condition.—This was good, her nutrition has not suffered, and apart from the pain she does not regard herself as sick. One feature is striking, the occurrence of *fever*. You will notice the temperature chart shows an irregular fever. For this

we could not find any other cause than syphilis, and the disappearance of the fever under treatment goes to support this view. We are all apt to forget that syphilis may be the cause of continued fever, and this may lead to unfortunate mistakes.

Pain.—To this particular attention should be given, as it is an important symptom in syphilitic disease of the aorta or myocardium. The pain in aortitis is referred to the upper sternum or beneath it, and, as in angina, there may be radiation to the shoulder and arm of either side. In this patient the pain was not referred to other zones. The degree of pain varies greatly; it may be more or less constant or come in attacks. In this patient the pain has been fairly constant, but has never been so severe as to require morphin. Of particular interest is the fact that this patient described two varieties of pain, the one referred to the upper sternum and the other to the precordium. She indicated the fourth left interspace inside the nipple line as the area when the latter was most marked. The explanation of this we must seek in a syphilitic myocarditis. You have seen several patients presenting the same condition.

The physical signs which are present in this case are marked. The most important are made out by inspection and percussion. There is a very evident pulsation in the neck. There is a well-marked visible impulse in the first right and the first and second left interspaces. A visible impulse in the second left interspace need not be of any special significance; it is common enough in thin-chested individuals. But it is a very different story when seen in the other interspaces, and usually means some aortic disease. The aorta can be felt in the suprasternal notch. Before giving too much importance to this as a sign of aortitis be sure that the position of the diaphragm is not higher than normal, as this may result in the aorta being situated higher than normal. On percussion you see a marked outline of dulness, measuring nearly 9 cm. across in the first interspace and nearly 8 cm. in the second interspace. On auscultation there is nothing of particular importance in this patient. Some would disagree with me in this and lay stress on the systolic murmur, but it is easy to draw conclusions which are not warranted from a systolic aortic mur-

mur. In some cases we may have a ringing, musical, aortic second sound which is often characteristic. Some have raised the question as to whether this musical sound is peculiar to syphilitic aortitis. Personally, my belief is against this, as I have heard it in patients in whom all the evidence was against syphilis, but there should always be the mental reservation that it may have been present. It is worthy of note that if aortic insufficiency is present this curious musical quality may characterize the diastolic murmur. Associated disease of the aortic valves causing aortic insufficiency should always be looked for with care. In this patient we find no evidence of it.

Radiographic Findings.—Evidently these give us positive information, and either by the plate or fluoroscopic examination the diagnosis may be confirmed. In this patient the aorta showed enlargement in the plate.

Pressure Signs.—As in aneurysm, these may be present and should always be noted. In this patient there was inequality in the pupils, which naturally might be ascribed to cerebral syphilitic disease. It disappeared under treatment. The alteration in the voice was possibly due to paralysis of the recurrent laryngeal nerve, although not proved, as the examination was not positive, and this also improved under treatment. Decrease in the pressure-signs due to aortitis is often noted if the patients are kept at rest for a time. The change in the signs over the upper part of the left lung were regarded as due to pressure.

The condition of the heart suggested myocarditis with dilatation. There was a wide-spread diffuse impulse which was better seen than felt. There was no localized apex-beat, and the area of dulness was increased both to the right and left. In both the tricuspid and mitral areas there was a soft systolic murmur which disappeared under treatment. The decrease in the signs of dilatation was very striking. The pulse-rate, between 100 and 140 at first, later fell to between 70 and 80. The blood-pressure rose from 108 to 120.

Prognosis.—What is the outlook in syphilitic aortitis? As regards the local change, we cannot hope for any marked improvement. The pain we can influence markedly, but the aorta

is probably damaged permanently. In some patients it has seemed that the size of the aorta had decreased slightly, but this is difficult to prove. Longcope has published some interesting figures as to the results of treatment in syphilitic aortitis. Among 31 patients, while 25 showed temporary improvement, yet relapse was the rule, and only 9 of the series were known to be alive; over half were dead. The duration of life is not given. An important element in the prognosis is the state of the heart muscle. This really is the main factor in estimating the future. If there is serious myocardial mischief, often syphilitic in these cases, the outlook is very grave for the immediate future and altogether bad for the remote future. It is possible that early diagnosis and very active treatment may improve the prognosis. If the patient survives the acute stage the prognosis then becomes that of chronic aortitis. It is altogether unlikely that such an aorta can ever be returned to normal. As to duration of life, unless an aneurysm forms subsequently it is not probable that the aortic condition in itself makes much difference, but the chance of disease of the coronaries must be remembered.

2. **Aortitis and Rheumatic Fever.**—You will not find much mention in the text-books of involvement of the arteries in rheumatic fever. This seems surprising when we consider the frequent involvement of the heart. The studies of Klotz on the arterial changes in rheumatic fever are of special interest. He describes a fairly typical lesion in the aorta, most often seen in the arch, less often in the descending thoracic, and rarely in the abdominal aorta. The main histologic change is in the media, in which the arterioles show an edematous perivascular infiltration with aggregations of lymphocytes and plasma-cells. The elastic fibers in their vicinity are interrupted and look as if they had been broken mechanically. The muscle elements of the media in the neighborhood of the vasa vasorum have in part disappeared. There is also considerable change in the adventitia. The capillaries are congested and the connective tissue loose and edematous. There is considerable cellular infiltration of lymphocytes and plasma-cells. In the more chronic cases the changes found were particularly in the form of loss of muscle and elastic

elements. In some instances the loss of tissue is quite marked. The process of repair is by fibrous change, which is described as a chronic productive mesaortitis. In view of this, it is not difficult to see that diffuse dilatation of an aorta so altered is a natural sequence of the changes in the walls.

This patient illustrates very plainly the clinical picture of a marked dilatation of the aorta with rheumatic fever.

CASE II.—The patient, aged twelve, admitted June 19, 1916, came complaining of discomfort in the chest, shortness of breath, and pain about the heart.

Past History.—For a number of years she has had attacks of tonsillitis at intervals. In June, 1915, following a rather severe attack of tonsillitis, she had a sharp attack of rheumatic fever and spent some time in a hospital, where she was told that the heart was diseased. After a stay of three months in the hospital she left in fairly good condition, and felt comparatively well, but noticed that she had shortness of breath if she ran up stairs. In February, 1916, she again had a severe attack of tonsillitis accompanied by a good deal of thoracic pain and shortness of breath. She spent three months in the hospital, and during this time the tonsils were removed under general anesthesia.

Present Illness.—After discharge from the hospital in May, 1916, she felt very well and did not have any shortness of breath for a couple of weeks. Then the difficulty in breathing returned, and she had an attack of severe pain referred to the heart. These attacks have returned, and she usually has one every two or three days. They generally come on at night, last perhaps an hour, and they are quite severe during this time.

Examination.—The patient is well nourished, has a good color, but seems to be underdeveloped for her age. The lungs show a clear percussion-note throughout. The breath sounds are harsh everywhere, and there are a certain number of râles at the bases. The thorax shows well-marked precordial bulging with a wide-spread visible impulse. The apex-beat is difficult to determine, but is probably in the sixth interspace, about 12 cm. from the midline. The heart dulness opposite the fourth interspace extends 3.5 cm. to the right and about 12 cm. to the left.

At the apex she shows a cycle of murmurs, but a diastolic murmur is heard with unusual loudness. At the base there is a loud intense diastolic murmur. The aorta can be seen projecting in the suprasternal notch and showing extreme pulsation. There is an unusual grade of pulsation in the neck; the position of the subclavians is quite high and they also pulsate markedly. There is dulness over the manubrium, and in both the first and second right and left interspaces, with marked visible pulsation in all four interspaces. The blood shows Hb. 81 per cent., red cells 5,400,000, leukocytes 10,000. The patient occasionally has attacks of severe pain. These she refers to the region of the heart, sometimes pointing to about the fifth interspace inside the nipple line, and occasionally pointing to the manubrium as the point where she feels the most pain. With these attacks she suffers a great deal of discomfort and the pulse-rate usually increases markedly. The dyspnea is marked and occasionally there is a tendency to syncope. In addition, she shows occasional attacks which only last for a few minutes, in which she refers the pain to about the left costal margin. In these attacks she will toss about the bed and sweat profusely. Her blood-pressure on admission was systolic 150, diastolic 90. It varied somewhat from time to time, but was usually a little below this, averaging 120 to 140. During the latter part of her stay it was sometimes down to about 110. The *x*-ray plate showed very marked enlargement of the heart and of the aorta.

The pulse-rate while she was in the hospital was very variable; sometimes remaining at about 90 to 100 for some days and then running up to 120 and 130. The cardiac condition improved decidedly, but the aorta remained practically in the same condition.

Remarks.—It is evident that as regards the essential condition in a patient such as this, damage to the heart itself is all important and probably the aortitis has little influence. It was not always possible to be absolutely certain of the seat of her pain, but apparently she had attacks of two kinds—one referred to the heart and the other to the aorta. On discharge her condition was wonderfully good, she had excellent compensation,

but the aortic condition was practically unchanged. The future in a condition such as this depends almost entirely on the condition of the heart. The aorta will probably remain unchanged.

The next patient illustrates the difficulty that may arise in making a definite etiologic diagnosis as to the cause of an aortitis.

CASE III.—The patient, a colored man, aged twenty-five, was admitted to the Pennsylvania Hospital on November 23, 1916, complaining of shortness of breath and pain in the region of the liver.

Previous History.—At the age of twelve he was in this hospital for eight months with endocarditis, but he gives no definite history of rheumatic fever. There is a history of an attack of chorea before this. He apparently has been fairly healthy in recent years. He states that he formerly used alcohol to excess, but has not used any for a year or two. There is a history of an attack of gonococcus infection and of chancroid, the exact date of which he does not know.

Present Illness.—As regards his present illness, he states that about a month before admission he began to have swelling of the feet. Following this there was fever, and he thinks that he had some chills. He then began to have severe pain in the region of the liver and following this a great deal of shortness of breath.

Examination.—The patient shows marked dyspnea without very marked cyanosis. There is diminished expansion of the right side of the thorax with dulness in the lower part, apparently due to hydrothorax, with many coarse râles at the left base. You can see an unusual fulness of the neck, which looks like a collar of edema, with the veins standing out prominently. You can see a very wide-spread visible cardiac impulse. The apex-beat is in the seventh interspace 17.5 cm. from the midline. No shock or thrill is felt. Opposite the fourth interspace the dulness extends 4 cm. to the right and 14 cm. to the left. There is well-marked dulness to the right and left of the manubrium. At the apex a continuous cycle of murmurs is to be heard. The systolic murmur is not particularly loud. In the tricuspid area there is a very intense systolic murmur, much louder than that heard at the apex. At the base there is a well-

marked to-and-fro murmur, but the systolic is not carried to the vessels of the neck. The aorta can be readily felt in the suprasternal notch. There is marked dulness in the first and second right and left interspaces with marked visible pulsation. This is also very evident in the neck. On palpation there is a well-marked diastolic thrill at the base. The pulse is 132, small and collapsing. The systolic pressure is 128, diastolic 60. The Wassermann reaction is very strongly positive.

It is evident that this patient shows very marked evidence of disease of the mitral, tricuspid, and aortic valves, with marked hypertrophy and dilatation of the heart, and extreme dilatation of the aorta.

The problem arises as to the explanation of his aortitis. He had chorea as a child, and we know that at the age of twelve he was in this hospital with endocarditis involving his aortic valve. This may well have been from rheumatic fever, because we should always remember that in childhood arthritis is the exception in rheumatic fever and endocarditis the rule. In addition, he has had a luetic infection. It is of interest to try and decide whether his aortitis dates from the infection in childhood or is syphilitic. In this connection the notes of his admission to the hospital seven years ago are of interest. At that time he had definite evidence of enlargement of the aorta with a loud double aortic murmur. In view of the definite evidence of aortitis many years ago and the endocarditis beginning early in life, there seems a strong probability that the aortitic disease is not luetic, or, at any rate, that in the first place it was not luetic. Naturally, we cannot exclude the possibility that a damaged aorta may have been attacked by the spirochetes.

The patient did not respond to treatment, his condition rapidly became worse, and he died on November 28th. At autopsy marked chronic endocarditis of the mitral and aortic valves was found, and, in addition, an acute fresh process. Both ventricles were very much hypertrophied, and all four chambers were markedly dilated. The murmur at the tricuspid area was due probably to relative insufficiency. The aorta was very greatly enlarged and showed marked atheroma, but

in the gross specimen it did not suggest syphilis. Dr. Ellis studied the aorta with particular care with reference to this point, and expressed the opinion that the aortitis was not syphilitic. The duration of the aortic condition would seem to me to support this.

Syphilitic aortitis is a serious condition, and the duration of life after it is established is probably not very long. As this patient did not have any proper treatment and yet lived for so long with the aortic condition, we may regard this as an additional point against syphilis.

CLINICAL FEATURES OF AORTITIS

Some of the clinical features of aortitis are worthy of notice. Among those of special interest are the pressure effects, which in many ways are like those of aneurysm except that they are less frequent and less marked.

The Pressure Effects of Aortitis.—(*a*) Of especial interest are signs in the *circulatory system*. In the last patient you noticed the marked swelling of the neck and the fulness of the veins. This latter may be partly due to back-pressure from the right auricle, but the same thing is seen in patients with aortitis without any cardiac failure. In another patient you saw the marked distention of the veins of the neck and arms and those about the shoulders. This is due to interference with the flow of blood to the auricle. The pulses in the arms may be different both in volume and blood-pressure. Some would ascribe the inequality of the pupils to circulatory disturbance. This seems more reasonable than to regard it as always due to pressure on the sympathetic nerves. Alteration in the blood-supply readily affects the pupil.

(*b*) *Respiratory System.*—In the first patient we regarded the difference in signs in the upper thorax as due to pressure, exactly as we may see in aneurysm. This is a point in diagnosis well worth attention. Some of you saw in the Department for Diseases of the Chest a patient sent in as a case of advanced pulmonary tuberculosis in whom the signs were due entirely to the pressure of a thoracic aneurysm. A *tracheal tug* is not uncommon in aortitis, but is not present in any of these patients.

(*c*) *Nervous System.*—The pain in aortitis is often a striking feature, and it is well to remember that it may closely simulate that of angina pectoris. In some cases who can say that it is not angina pectoris? In other cases the character of the attacks of pain is different. The pain persists for a considerable time, is not so severe as in typical angina, and there is not the evidence of severe agony which the true attack presents. If the pain is referred this may be down the right arm perhaps as often as down the left; sometimes it is referred to both arms, a point which should always suggest aortitis. In other patients there is complaint of numbness referred to the shoulders or arms. In rare cases this can be produced by firm pressure over the upper sternum. A recurrent laryngeal nerve paralysis may occur, and in other patients, as in one whom you have seen, there may be an alteration in the voice without any definite paralysis being found.

(*d*) *Esophagus.*—Complaint of difficulty in swallowing is rare, but has occurred.

THE DIAGNOSIS OF AORTITIS

This does not offer any great difficulty, as a rule, if one knows that such a condition exists. A few days ago some of you heard a visitor in the ward declare, I am afraid in rather a heated manner, that he had been thirty years in practice and had never "seen" a case of aortitis. This statement was not quite correct, although not purposely so; he had "seen" many of them, but had not "recognized" them. This is something which we are doing constantly, so do not pass a harsh judgment on the visitor. Many impressions fall on your eyes and mine and get no farther. To know that such a condition exists and to be on the watch for it are great aids to begin with. Very few of us observe what we have not been trained to observe. "The eye sees only what it is trained to see."

Inspection.—The fulness of the neck and the dilatation of the veins in the neck, arms, and about the shoulders are important as suggesting some obstruction to the return of blood. The visible arterial pulsation may be extremely marked and

the subclavians may be seen above the clavicles or the carotids may show a tortuous course, in either case causing unusual pulsation. Their point of origin is higher than normal and they are therefore displaced. In a rare case there may be a distinct pulsating tumor. If the aorta can be seen above the top of the sternum the diagnosis is almost definite. Pulsation in the episternal notch is very common in aortitis and should be looked for as a routine. The other situations where pulsation should be noted are in the first and second right and left interspaces. Pulsation may be marked in any one, all four of them, or in any combination. Do not attach too much importance to pulsation in the second left interspace, as it does not necessarily have any significance. Good light is important for proper inspection. Your eyes should be about on a level with the patient's thorax, and usually it is best to have the patient flat, although in a few cases the impulse is more marked with the patient sitting. The second right interspace is the most common seat of pulsation, then the second left, first right, and first left in order. The pulsation is usually more visible than palpable and can rarely be felt. In some cases there is a heaving impulse of the manubrium and occasionally the inner end of one clavicle is lifted.

Palpation.—It may be possible to feel the aorta in the suprasternal notch or to palpate the subclavian and the often tortuous carotid arteries. The heaving impulse of the manubrium can be felt occasionally, but usually it is more visible than palpable. A shock, generally diastolic, or a thrill, also usually diastolic, is sometimes palpable. The visible pulsation in the interspaces can rarely be felt.

Percussion.—This gives us information of much importance, and if inspection has failed to give a clue to the condition, percussion should do so. If you begin percussion by determining the highest point of cardiac dulness at the left sternal margin you may find that there is no beginning point of dulness as it extends up to the first rib. This suggests aortic dulness, and then by coming in from the outer part of the first interspace with the finger at right angles to the ribs you can readily determine dulness on each side of the manubrium. In nearly every

case of increase in size of the aorta of any extent some dulness will be found. The width of this varies from 7 or 8 cm. to 14 cm. and it is usually greater in the first than in the second interspace. It may be more marked on the right or left; I have usually found it more marked on the left.

Auscultation.—In some cases there is a characteristic quality of the second sound, or of a diastolic murmur if present, which may suggest the diagnosis. This is a musical bell-like sound which is quite distinctive, and which I have never heard in any other condition. Once heard, it is easy to recognize it again. It is quite distinct from any accentuated quality. In addition, the second sound, or a diastolic murmur, is heard with unusual loudness high up over the manubrium, in the suprasternal notch, and over the carotids. Some place much stress on a systolic aortic murmur, but I hesitate to agree with this, and do not believe that any definite conclusion can be drawn from it. Systolic murmurs at the base should always be regarded with doubt unless there are other signs.

Blood-pressure.—This may be high or low, but in the majority is normal or below normal. This is particularly true of the chronic cases.

Results of x-Ray Examination.—This may be the deciding point in a doubtful case. There is increased width of the aorta. With fluoroscopic examination the shadow varies in size, but persists between pulsations.

Of other conditions which may cause difficulty, *aneurysm* is the most important. In this the pulsation is more readily palpable and may be stronger than that of the heart. The area of dulness is more regular in aortitis than in aneurysm and is usually continuous with the cardiac dulness. The peculiar quality of the second sound if present is characteristic of dilatation. In rare cases the *x*-ray examination must decide. *Intrathoracic tumor* rarely gives difficulty, as the pressure signs are more in evidence. The *x*-ray examinations should settle the point if there is doubt.

Malposition of the aorta may simulate dilatation, but, as it usually occurs with deformity of the spine or shrinking of one

side of the thorax, the recognition should not be difficult. In some patients a high position of the diaphragm may result in the heart and aorta being higher than normal. This may cause difficulty in the *x*-ray examination as well as in that by the ordinary methods.

One disease may be suggested by the attacks of pain, namely, angina pectoris. In reality, who can say that the attacks of pain in aortitis are not angina? There is no question that proper treatment of aortitis, especially the luetic variety, sometimes results in complete disappearance of the pain. The pain in aortitis is rarely as severe as in angina and may persist for hours; it may be referred down the right arm, and in some patients is felt in both arms. One point is of special interest, the pain of angina is aggravated by exertion; that of dilatation, certainly in its milder forms, is frequently relieved by moderate physical exertion. This is supported by the observations of many patients. One man who has had aortitis for many years, in etiology apparently not luetic, and who has studied his symptoms very closely, tells me that when he plays golf there is nearly always some discomfort until he has played two or three holes, after which he is quite comfortable and goes around the full course in perfect comfort. He is firmly of the opinion that with moderate exercise his general condition is better than when he is quiet. His blood-pressure has never been over 130 and averages 120. In any case of doubt as to the character of the pain it is wise to regard it as due to angina.

The frequent association with *cardiac disease* may lead to the overlooking of the aortic lesion. This is not surprising, as the cardiac disorder is sufficient to account for the symptoms. Undoubtedly this is responsible for the fact that the aortitis of rheumatic fever is so rarely recognized as attention is fixed on the heart. A careful examination should prevent this mistake.

The diagnosis should be carried beyond that of the anatomic lesion—aortitis—to the causal factor if possible. Unless the aortitis is very clearly from rheumatic fever one should hold syphilis in mind until the contrary is proved. A negative Wassermann reaction in the blood should not be regarded as

positively excluding syphilis. The etiologic diagnosis has a bearing on prognosis. There seems good reason to consider the outlook in syphilitic aortitis as distinctly worse than in that due to other causes. How much we can influence luetic aortitis by early recognition and intensive persistent treatment remains to be shown. Certainly the patient should have the chance. In general, the outlook in syphilitic aortitis is not good for the ultimate result. As for the other varieties, it appears that the lesion is compatible with many years of life and fair activity. The condition of the heart is always important.

TREATMENT

As to *treatment*, that of the syphilitic variety has been discussed. There is no special treatment of the other varieties. The measures usually adopted for arteriosclerosis are indicated, and particular attention should be paid to the state of the heart. If pain, dyspnea, distress, and marked pressure signs are present, rest is indicated, but this does not need to be for a very long period, two weeks are usually sufficient. In the laboring classes an occupation involving severe strain should be given up if possible. It is essential to keep the bowels freely open, as straining at stool is harmful. Of drug treatment the giving of iodid is useful, as a rule, in small doses (gr. xv to xxv a day) and for a considerable time. Digitalis is not indicated for the aortic condition itself. In some of the patients who have pain the giving of small doses of a vasodilator (nitroglycerin or sodium nitrite) may give relief, but morphin should not be withheld if the pain is severe and not relieved by other measures.

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CLINIC OF DR. ALFRED STENGEL

HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

THE CLASSIFICATION OF CHRONIC NEPHRITIS AND THE RELATION OF INFECTION TO KIDNEY DISEASE

GENTLEMEN, I wish to present for discussion today a case of nephritis in which there is a probable relation to localized infection, and to discuss with you the possibility of curing such nephritis by removing the infected focus. I shall first ask Mr. A. to read the history of one of these cases.

MR. A.: John X, aged twenty-eight, a machinist, was admitted to Ward D on account of swelling of the hands, face, legs, and to a slight extent the back, and on account of general weakness and loss of appetite.

History of Present Illness.—Until three or four weeks ago the patient had been in his usual health and had been regularly at work without any thought of illness. He then got what he calls a "sore throat" and had rather high fever for a day or two. The doctor who was called in spoke of the condition as acute tonsillitis. The patient says he could not swallow food or even liquids without great pain in his throat, and he felt sore and rather stiff all over, especially in his back and limbs. After two days he began to improve, and in four or five days was practically well so far as his throat was concerned, but remained weak. Somewhat later, while still about the house, feeling too weak and miserable to go back to work, he noticed that his face and hands were a little puffy. This increased and extended to the body and legs. The doctor was again called in, when he asked for a sample of the urine, which he examined, and reported as showing signs of disease of the kidneys. The patient was put to bed and given

various remedies, but the swelling did not subside, and he was referred to the hospital for treatment.

Past Medical History.—The patient has always been in good health since childhood. He remembers vaguely some illnesses when he was quite young, but does not recall any that were specially severe. He has had no severe illness since then. At various times he has had sore throat, but does not think he suffered more in that way than most boys whom he has known. He denies venereal infection.

Social History.—Since he left school he has worked in a machine-shop at lathes and other machines, but never at specially heavy jobs. He was not exposed to unusual degrees of heat in his work, nor to dampness and cold. His habits have been good as to diet, the use of alcohol, and tobacco.

Family History.—Negative.

DR. STENGEL: What would the history suggest to you regarding the diagnosis?

MR. A.: The patient probably has nephritis, with moderate nephritic edema.

DR. STENGEL: Upon what facts do you base this suggestion?

MR. A.: The history of a general slight puffiness or edema without any history of shortness of breath, cardiac disturbance or cyanosis, and without any account of chronic failing health or anemia would indicate kidney disease as the most likely cause of the edema. In addition, the examination of the urine made by his physician seems to have shown evidence of nephritis.

DR. STENGEL: You have reported nothing in your history regarding the quantity of the urine. What are the facts about this?

MR. A.: The patient had not noted any special change in the quantity of urine. Since he has been under my observation in the ward the daily amount of urine has varied between 450 and 850 c.c. This is, of course, a considerable diminution.

DR. STENGEL: Please have the patient brought in and give us the results of your physical examination.

MR. A.: The patient is a sturdily built young man. His face is rather puffy and there is slight edema of the hands and

forearms, the feet and legs, and a little at the back of the thighs and in the tissues of the back. The skin is distinctly pallid; this is especially noticeable in the face, on the anterior surface of the chest and abdomen, and in the legs. The lips and conjunctiva also are somewhat paler than normal. The tongue is coated, the teeth in fair condition, and the gums normal. The tonsils are large and rather irregularly indented with deep crypts. The mucous membrane of the pharynx is rough and granular. The superficial lymphatic glands of the neck are not palpable; those in the inguinal region are slightly palpable; those in the axilla and epitrochlear region are not felt. Examination of the thorax is negative. The heart extends 10 cm. to the left of the middle line, 3 cm. to the right, and the dulness at the base, at the third rib, is not increased in width. The heart-sounds are normal. The pulmonary resonance and the breath-sounds also are normal. The abdomen is not distended; the liver and the spleen are not palpable. Nothing abnormal could be felt in the abdomen.

The pulse is 78, the respiration 16, the temperature 98.1° F. The blood-pressure: systolic 130, diastolic 75.

The blood examination showed: R. B. C., 4,500,000; W. B. C., 8200; hemoglobin, 78 per cent.

The urinary examination showed: Total quantity, 800 c.c. Specific gravity 1018, acid, albumin—a heavy cloud on boiling and addition of acid, no sugar; microscopically, many hyaline, light and dark granular casts, some large granular cells, and a moderate number of leukocytes.

DR. STENGEL: What conclusions would you draw from these facts as to the diagnosis?

MR. A.: The patient has chronic nephritis with edema.

DR. STENGEL: What type of nephritis?

MR. A.: Chronic parenchymatous nephritis.

DR. STENGEL: Before discussing your diagnosis it may perhaps be well for me to outline the classification of nephritis that works best from the standpoint of prognosis, and that seems to correlate clinical and pathologic findings. The old distinction of parenchymatous and interstitial nephritis has

been found defective in practice, though it has become so entrenched that it is important to compare any new classification with it to see what advantage has been gained, and how the old and newer terms correspond.

In studying the histology of damaged kidneys we find that the pathologic changes may be grouped under three heads: (1) Glomerular change which varies in intensity and may present itself as hemorrhage or exudation in the space between the capillary tuft and the outer limiting epithelial lining of the sac, proliferation and degeneration of the epithelia, hyalinization, atrophy or sclerosis of the Malpighian body, thrombosis of the capillaries of the tuft, and in later stages sclerotic thickening of the outer wall of the capsule. These changes may be variously grouped and few or many or all of the Malpighian bodies may be involved. (2) Tubular changes. The epithelial cells lining the tubules, especially in the important convoluted portion, may be swollen and cloudy or extensively degenerated, and sometimes removed from their basement membrane or atrophied and distorted. (3) Sclerosis in the form of concentric layers of fibrous tissues surrounding the diseased Malpighian bodies, or as fibrous thickening and condensation of the intertubular tissues is a late result of either the first or second group of changes.

Aside from these three groups of changes which for purposes of classification are fundamentally important, we find in the nephritic kidney more or less extensive changes in the renal blood-vessels (arterioles) and in the capsule. In acute cases the distribution of the lesion is practically the same as in the chronic, though congestion, hemorrhage, and exudation of albuminous fluid within the capsule or cellular infiltration in the intertubular tissues are conspicuous.

It must be obvious that in a compact and complicated glandular structure such as the kidney a pathologic lesion is not likely to confine itself to one of the histologic elements to the exclusion of the adjacent parts, and clinicopathologic experience shows that combinations occur in renal disease which make a rigid classification of definite forms untrustworthy.

A renal disease that involves the glomeruli mainly is called

glomerulonephritis; one that affects the tubular epithelium mainly may be called *tubular nephritis*, though the name *degenerative nephritis* is also used in cases of mild type in which the pathologist hesitates to classify the epithelial disease as inflammatory. Such terms as "nephropathy" or "nephrosis," which have been applied in the same cases and for the same reason, do not help us much. One may just as well speak in plain English and say kidney disease.

When terminal sclerosis occurs around the glomeruli and between the tubules the condition may be called *chronic interstitial nephritis*, but as this term has in the past had a rather fixed clinical significance that notoriously failed of histologic vindication, it should either be used in a strict pathologic sense, or the shorter and better name, *renal sclerosis*, should be used. There is a type of acute renal disease that is strictly an *acute interstitial* (non-suppurative) *nephritis*, in which round-cell infiltration is found abundantly between the renal tubules. This is mainly of pathologic interest, as its clinical manifestations are little known.

We may, then, classify the fundamental forms of nephritis as—

1. Tubular nephritis.
2. Glomerulonephritis.
3. Renal scleroses.

Between these lie many combined forms and transitional types that have made accurate renal diagnosis difficult, and have made it especially difficult for the clinician to state the prognosis in a given case. During recent years, and very largely as a result of their interest in the newer renal functional tests, clinicians have reviewed the whole matter of the clinical and pathologic classification by comparing the clinical manifestations and functional tests in different cases, and studying these closely in the light of the histologic findings after death. Volhard and Fahr ("Die Brightsche Nierenkrankheit," Berlin, 1914) published a very illuminating monograph covering this ground, and about the same time Drs. Austin, Pepper, Wolferth, Jonas, and myself were studying the matter in much the same

way here, and Dr. Christian and his associates at Harvard were making very valuable contributions from the Brigham Hospital.

While it cannot be said that there is as yet entire agreement regarding the definition of different types, in a general way considerable progress has been made in the direction of establishing a classification that will work out, provided the clinician remembers that transitional forms are frequent. A hasty decision as to the type of a case (and it may be remarked in advance that accuracy in prognosis is especially dependent upon the recognition of the type of the disease) may lead to error that could have been avoided by a more careful study of the history and progress of the case.

Now let me place before you in a very brief outline the clinical distinctions seen in the three types of disease.

1. Tubular Nephritis (*Degenerative Nephritis, Nephrosis, Nephropathy*).—Mild tubular degeneration occurs in a high proportion of cases of various infectious diseases, even the milder ones. It is hardly worth while attempting to separate those which are merely toxic degenerations of the epithelium from those which may more properly be regarded as inflammatory. I prefer to think of them as mild and severe types of tubular nephritis. In an analysis of 342 of our cases of typhoid fever mild tubular nephritis was present in 42 per cent. of the cases, and more severe in 5 per cent. Please remember that many clinicians would not at all regard these mild cases as nephritis; but I believe it is more accurate to do so, and we must not mislead ourselves with the false notion that they are not nephritis because they all recover speedily, and because nephritis, as we usually picture it to ourselves, is a very serious affair. One might just as well deny that there are mild as well as severe or destructive forms of conjunctivitis. Tubular nephritis, however, is not always mild. Certain mineral poisons, notably bichlorid of mercury and chromium salts, cause very serious renal disease that is strictly tubular in character; and some of the infections, notably cholera and yellow fever, may have a like effect. Between these extremes of very mild and very severe tubular nephritis are cases that tend neither to the speedy resolution of

the former nor the fatal outcome of the latter. In these cases the disease becomes subacute or chronic, though it often increases in severity as time goes on. The symptoms in the milder cases are negligible, and the condition would be unrecognized if careful observations of the urine were neglected. The quantity of urine is reduced, the specific gravity is usually increased, and there is found a small amount of albumin, or sometimes considerable albumin with hyaline and light granular casts, less commonly cell-bearing casts. No special change occurs in the symptoms of the infection with which such mild tubular nephritis associates itself.

In severe cases the urinary findings are much the same. The albuminuria is more marked and casts of all sorts are commonly presemt. Oliguria is more pronounced. The patient presents a pallid, often a waxy appearance of the skin, has a coated tongue, frequently lack of appetite and digestive disturbances, and is weak and depressed. The pronounced nephritic indication in such cases is edema, which may become so extensive as to constitute a general anasarca. There is little tendency to the other marked nephritic complication—uremia. For a long time the patient may show increasing edema with decided reduction in the quantity of the urine, but without any tendency to uremia. Indeed, the fatal end of such a case may be reached as a result of accumulating dropsical effusions in the serous cavities, and increasing weakness without the least evidence of uremia. Not rarely, however, uremia may develop as a late feature and terminate the clinical story. From the beginning to the end these cases show little tendency to elevation of blood-pressure. Often it is definitely subnormal. I shall not pause at present to discuss the results of functional tests, but will allude to them later. The conspicuous features of these cases, then, are: the pronounced albuminuria with abundance of casts, the tendency to edema, the oliguria and relatively high specific gravity of the urine, the absence of high blood-pressure and of signs of uremia. The patient may recover from the edema and all active symptoms, and may subsequently relapse, perhaps several times at long intervals. I have seen numbers of cases that behaved in

this way. This contrasts rather sharply with the history of glomerulonephritis, which is a more rapidly progressive condition, with nothing approaching the same probability of remission.

2. **Glomerulonephritis.**—This type is much less frequently associated with a distinct antecedent cause, though the violent acute nephritis that occurs in scarlet fever, pneumonia, streptococcus infections, and less frequently in other infections, is acute glomerulonephritis. Far more frequently glomerulonephritis is recognized in its chronic stages and the etiology and early history are obscure. This circumstance suggests the possibility of an earlier unobserved acute attack with partial recovery, or repeated slight involvements until the damage has become massive.

In the acute stages of glomerulonephritis the symptoms, in brief, are oliguria, with marked albuminuria and abundant casts, often considerable blood, even amounting to hematuria, high specific gravity of the urine, edema, moderate elevation of blood-pressure, tendency to uremia. The patient's general appearance may be not unlike that seen in the dropsical cases of tubular nephritis, but the higher blood-pressure, the greater albuminuria, the microscopic findings in the urine, and the tendency to uremia are contrast features.

Such cases may gradually clear up and partial or perhaps seemingly complete recovery ensue, leaving a subacute or chronic glomerulonephritis, without marked symptoms. On the other hand, an insidiously developed subacute or chronic glomerulonephritis may be encountered. In either case the symptoms are rather indefinite. Often the patient complains of nothing at all, but for some reason a physical examination may be made and elevation of the blood-pressure be discovered. Sometimes in addition to this slight polyuria and general, though indefinite, ill-health may also call attention to the trouble. This stage of glomerulonephritis, however, is confessedly one that is easily overlooked.

Late or chronic glomerulonephritis presents rather marked symptoms. Usually the patient is rather pallid, though more

yellowish in color than in the edematous forms of tubular nephritis, and there is apt to be emaciation and sometimes a wrinkled condition of the skin, which may give the patient an appearance not unlike that of malignant cachexia. Digestive disturbances, coating of the tongue, a heavy, unpleasant odor of the breath, general weakness and circulatory disturbances, probably in large part secondary to the elevation of the blood-pressure, are encountered. The blood-pressure in these cases reaches excessive heights; a systolic pressure of 200 to 240 being not unusual, and a diastolic figure of from 120 to 160. Some cardiac enlargement, and sometimes very distinct hypertrophy of the left ventricle with a loud muscular systolic heart-sound, and in later stages, when cardiac compensation begins to fail, an apical systolic murmur, are the cardiac features of such cases. There is usually polyuria; sometimes this is quite marked, and the quantity of the night urine in particular is frequently excessive. The specific gravity is rather definitely fixed at from 1011 to 1013; traces or small amounts of albumin and hyaline and faintly granular casts are present, but in some instances several examinations of the urine may be made before either albumin or casts are discovered, and in many cases an occasional examination of the urine shows neither albumin nor casts. The patients frequently complain of failing vision, and the ophthalmologist discovers the evidences of genuine albuminuric retinitis when the case is advanced to a certain point. The disease progresses more or less rapidly, and toxic symptoms significant of a uremic state sooner or later supervene. A large proportion of these cases ultimately die with outspoken uremia, though some succumb as a result of apoplexy or cardiac failure, but even these are likely to present uremic symptoms before the fatal end takes place. Dropsy is a relatively rare event in this type of chronic nephritis, though in the terminal stages, when the circulation has failed completely, dropsy of the feet and legs and even a generalized edema may occur.

The contrast in the picture of such a case with that of tubular nephritis in any of its grades of severity is quite striking, and if it were not for the occurrence of mixed forms or combination

forms in which some of the elements of a glomerulonephritis and other indications of tubular nephritis occur simultaneously, the anatomic diagnosis would be much more readily made than is actually the case. A knowledge, however, that such transitional types are to be expected aids the clinician greatly in properly evaluating the symptoms presented in any case of chronic nephritis, however mixed it may be. In accordance with the prominence of such symptoms as edema, concentration of the urine, elevation of specific gravity, and multiplicity of casts on the one hand, or high blood-pressure, disturbances of vision, fixation of the specific gravity of the urine, and tendency to toxic or uremic symptoms on the other hand, will be the diagnosis of a tubular form of nephritis and a relatively favorable prognosis in the one case, or a glomerulonephritis, and a more serious outlook in the other case.

3. **Renal Scleroses.**—The term "renal sclerosis," as I have defined it, indicates simply the anatomic or histologic findings in a diseased kidney, and designates an end-stage in some other form of renal disease. It is not improbable, and it has been asserted by some of the pathologists that the acute interstitial non-suppurative nephritis of diphtheria and other infections may terminate in renal sclerosis, which would then be, indeed, a primary form of chronic renal sclerosis. It is more certainly known that in most of the cases of glomerulonephritis that have reached late stages considerable sclerosis occurs around the Malpighian bodies and between the tubules. Purely tubular cases of nephritis perhaps are less likely to go on to a stage of this sort, but mixed cases of glomerulonephritis and tubular nephritis undoubtedly frequently terminate in a contracting stage. Aside from these there is a form of renal sclerosis which apparently follows wide-spread arterial disease involving the smaller arterioles. These cases may have a prolonged clinical history in which symptoms of renal disease are not conspicuous, and may terminate in rather rapidly developed nephritis. On the other hand, they more frequently end in a cardiovascular death. The original arteriolar disease here referred to corresponds to that which was described by Gull and Sutton

under the name of "arteriocapillary fibrosis." In the terminal stages of this more or less pronounced renal sclerosis occurs. In a certain proportion of the cases, however, a complicating glomerulonephritis develops, and changes the whole clinical picture. I shall refer to this matter again a little later. Finally, among the cases of renal sclerosis we may place the renal atrophy of senile arteriosclerosis.

Thus we may summarize the possible forms of renal sclerosis as being:

1. Primary sclerosis following acute interstitial nephritis.
2. Secondary sclerosis following glomerulonephritis or mixed forms of nephritis.
3. The terminal sclerotic kidney following arteriolar sclerosis.
4. The atrophic kidney of senile arteriosclerosis.

Regarding the first form, one can say practically nothing. The existence of this type is rather a pathologic assumption than a demonstrated fact. The symptoms of renal disease in these cases are indefinite and uncertain.

The occurrence of sclerosis as a terminal event in glomerulonephritis or mixed nephritis does not materially alter the symptomatology of the preceding disease, although it may perhaps be said that in the mixed cases the supervention of sclerotic change gives to the case more and more the features of the glomerulonephritic type.

The symptoms of arteriolar nephritis are exceedingly interesting and important. In the first place, I wish again to point out that while I use this term for convenience, the symptoms are really not nephritic symptoms at all, as the kidney condition and certainly the kidney function are apparently unimpaired for long periods of time. The disease usually begins in the fourth or fifth decades of life, but may continue for many years. In one instance under my own observation there was good ground for believing that it had existed for upward of thirty years. The most marked clinical phenomenon is the high arterial pressure, and because of the relatively benign course of these cases the not inapt term "benign hypertension" has sometimes been applied to the condition, and "benign sclerosis" to

the form of renal disease that accompanies it. The appearance of the patient is often strikingly normal. The color may be good, digestion excellent, and except for some evidence of vascular hypertension, as indicated by throbbing circulation or undue tendency to fatigue, the patient would be unaware of any illness. The pressure may be quite as high, or even higher, than in marked instances of glomerulonephritis. But little change may be noted in the quantity of the urine, the tendency being perhaps toward slight polyuria. The specific gravity varies, and frequently I have observed that there is a pronounced difference in the morning and evening specimen. Sometimes very active secretion follows water drinking. Although I am not here discussing the results of the functional tests of kidney capacity, it may perhaps be well to remark that all such tests fail to indicate any reduction in the efficiency of the organ. Even severe dietary procedures fail to develop any blood retention of nitrogenous products. It is important to call your attention to the fact that there are not infrequently in these cases marked changes in the retinal arterioles, and sometimes retinal hemorrhages that could easily be mistaken for evidences of true "albuminuric retinitis." The latter may occur when a complicating glomerulonephritis becomes associated with the original arteriolar nephritis, and then possesses the same grave prognostic importance as that which attaches to albuminuric retinitis in any form of renal disease.

The symptoms in cases of renal atrophy of senile arteriosclerosis are largely those of the circulatory trouble, and very little attributable to the kidney. The discovery of traces of albumin and hyaline or granular casts sometimes regularly, more often at irregular intervals, is mainly important because upon this too frequently the erroneous diagnosis of a serious renal disease is based. The urine is apt to be somewhat excessive, its specific gravity low, but not so definitely fixed as in glomerulonephritis. The blood-pressure is generally somewhat elevated, though not excessively. In individuals of sixty to seventy years a pressure of 165 to 175 or 180 is not especially excessive. Sometimes, however, the pressure in these cases is constantly low.

The terminal event in these cases is cardiovascular as a rule rather than renal, but there may be sufficient renal disease present to occasion uremia or other renal phenomena when the patient becomes debilitated by increasing weakness or some intercurrent disease. This, however, is to be regarded as an accidental circumstance rather than as the usual course of events.

Let me now put together in tabular form the types of nephritis that we have so far considered:

1. Tubular nephritis:
   (*a*) Mild—with practically no symptoms except albuminuria and cylindruria.
   (*b*) Severe—with characteristic urinary findings and edema.
2. Glomerulonephritis:
   (*a*) Acute form—with dropsy, mild or severe hematuria, as well as a tendency to uremia.
   (*b*) Subacute or intermediary form—with scarcely any renal symptoms, but with pronounced elevation of blood-pressure.
   (*c*) Chronic form—with excessive blood-pressure, marked fixation of specific gravity of urine, tendency to uremia, disturbances of vision, and suggestive appearance of patient.
3. Renal scleroses:
   (*a*) Possible primary renal sclerosis following acute interstitial nephritis.
   (*b*) Secondary renal sclerosis following glomerulonephritis and mixed nephritis.
   (*c*) Arteriolar nephritis or benign sclerosis.
   (*d*) Arteriosclerotic atrophy of the kidney.

I have not placed "amyloid kidney" in this table, nor some other complicated and not altogether usual types. These may be ignored in our present discussion.

DR. STENGEL: Can you tell me, from looking at the table I have given you, which of the forms here set down would correspond to what you have elsewhere seen described as parenchym-

atous nephritis, and which forms belong to the group known as interstitial nephritis?

MR. A.: I think, in looking at the table, that tubular nephritis would be the form that is spoken of as parenchymatous nephritis, but I do not quite know how to place interstitial nephritis.

DR. STENGEL: If you will run down the table you will note that tubular nephritis, both in the mild and severe form, and acute glomerulonephritis, with its tendency to dropsy, correspond to the older description of parenchymatous nephritis. I suspect that in some cases even the intermediary or subacute form of glomerulonephritis might also be included. From that point down you will see that the different types of nephritis correspond to what in older writings was called chronic interstitial nephritis, and you will, therefore, see why the autopsy in so many cases failed to confirm the clinical diagnosis. Cases of chronic glomerulonephritis are strictly of the type of the chronic interstitial nephritis of literature, and in the earlier stages show histologically very little sclerotic change.

Mr. A., to come back to your diagnosis of the case, will you now indicate to me where, in the table I have outlined, you would place this patient's case?

MR. A.: Evidently, from the presence of edema and the absence of elevation of blood-pressure, you would call this a tubular form of nephritis. Apparently it is chronic because there is no history of blood appearing in the urine. I do not know whether this should be regarded as proof that this is a chronic case.

DR. STENGEL: In the acute glomerulonephritis of infectious diseases and toxemia and in the violent acute tubular nephritis caused by bichlorid of mercury and similar poisons one does almost invariably find more or less blood in the urine. It is not improbable, however, that many cases of acute tubular nephritis more or less severe in type may occur in the course of infections without blood. Certainly, mild acute forms do occur without blood, as we daily see in the reports of the urinary findings in cases of acute infections in our wards. Whether

or not an acute tubular nephritis with edema would occur without blood is not so easily settled, but I think you may regard it as possible.

What functional tests have been made in your patient?

MR. A.: Only the phthalein test, which showed an excretion of 30 per cent. of the phthalein injected within the two-hour period.

DR. STENGEL: There is evidently a reduction in the elimination of the phthalein, but not as great a reduction as is seen in glomerulonephritis. It is not my purpose today to discuss the various functional tests or their value in the diagnosis of nephritis, but one cannot at this day consider classifications of nephritis without making some allusion to this subject. On another occasion I shall refer specially to these tests. For the present I wish to call attention only to the fact that these tests are of great value in confirming diagnosis, and that their study and elaboration has done much toward clearing up the matter of classification of differnt forms of nephritis. As a matter of fact—now that such a fairly workable classification has been made out—this type of nephritis can generally be distinguished without recourse to any of the finer chemical tests, though these may be of inestimable advantage in gaging the progress of the case. The various functional tests may be classified as (1) studies of the power of the kidney to eliminate coloring-matters or various salts; (2) determinations of the amount of (*a*) nitrogen retention in the blood (urea-nitrogen; total non-protein nitrogen; creatinin); of (*b*) the plasma chlorid content; (*c*) plasma carbonates; (3) studies of the physical qualities and total excretion of the urine (specific gravity; power of the kidney to concentrate the urine), and (4) blood-pressure determinations.

The relatively slight reduction in excretion of phthalein and other coloring-matters and the absence of pronounced nitrogen retention in cases of tubular nephritis as compared with glomerulonephritis; and the retained power to concentrate the urine in the former as compared with the latter are distinctly helpful in diagnosis. The lack of excessive blood-pressure in tubular nephritis is a further point of distinction. For the present I

shall say nothing about the matter of plasma chlorids in the two forms. In the renal scleroses—except such as are secondary to glomerulonephritis—the results of functional tests lie midway between those found in tubular and glomerulonephritis. It is especially noteworthy, as I indicated before, that despite the high blood-pressure the renal functional tests give practically normal results in benign sclerosis. It must, however, always be remembered in connection with such functional tests that exceptions are not infrequent.

What suggestion have you to make regarding the etiology in your patient's case?

MR. A.: None of the usual etiologic features are shown in the history. The disease apparently began after an attack of fairly severe acute tonsillitis, and the patient has clinically enlarged tonsils with infected crypts. I suppose this must be the etiologic factor.

DR. STENGEL: What is your opinion regarding the influence of cold, of excessive use of alcohol, and other factors in the causation of kidney disease?

MR. A.: I understand that these are regarded as causes.

DR. STENGEL: In the course of my discussion of the various types of nephritis I have mentioned infectious and toxic influences, but have not undertaken any detailed reference to the etiology of nephritis. So far as cold and alcohol are concerned, the common belief is that these are potent factors, but one sees less and less allusion to these in scientific discussion, and I think you would do well to look upon them as being in the category of predisposing causes. Abuse of alcohol, combined with infection, probably accounts for many cases of serious kidney disease, but the direct effect of alcohol is by no means established. In recent years more and more attention has been given to the infections. As I have before indicated, tubular nephritis is a condition which accompanies practically all infections to a greater or less extent. So far as glomerulonephritis is concerned, the most severe acute types are those met with in scarlet fever, the septic infections, and pneumonia, but statistical studies and inferences drawn from the association of local in-

fection seem to indicate that organisms of the streptococcus group are largely concerned in the development of this form of nephritis, whether it be sudden or insidious in onset.

The frequency of renal disease in pregnancy, and persistent renal disease following pregnancy awaits satisfactory explanation. For the present we must recognize the clinical fact, though we cannot give a satisfactory explanation of it.

The study of chronic renal disease raises the question which is of rather fundamental importance in the matter of treatment—whether chronic renal disease is simply the progressive outcome of a pathologic condition initiated by some cause or other at an earlier period in the patient's life. The point is as to whether renal disease once started necessarily progresses until more and more of the kidney substance is involved. If we look over the list of so-called chronic disease we will find that except the chronic infections, such as tuberculosis or syphilis, many so-called chronic diseases are not chronic at all in the sense of progressive, continuing pathologic processes. In the case, for example, of valvular heart disease, the heart lesion is an after-result of an acute endocarditis, and the damage to the valve is done at and shortly after the time of infection. Subsequently the condition is not really a chronic endocarditis, but a damaged heart valve. Such a valve may become reinfected, but this is not what necessarily takes place in cardiac disease. The contractions and distortions of the valve may indeed increase after they have originally been started, but the extent oi the damage is practically established from the start. Perhaps the same applies to kidney disease. A certain amount of damage to glomeruli or tubules may be done by an infection or a toxic agent, and the areas so damaged may suffer more and more degenerative change or atrophy, but there is no special reason for believing that the disease extends to other portions of the kidney until it has become generally involved. It would seem more probable that in chronic nephritis repeated insults to the kidney occur, and that this explains the insidious onset of many eventually serious forms of nephritis. Precisely the same thing occurs in the case of chronic arthritis, some chronic ane-

mias, and the like. These are now quite generally accepted as being frequently dependent on local foci of infection. The damage done in the first place is slight, later it becomes more and more marked, and finally the end-result is a clinical condition that cannot be overlooked.

Applying these thoughts to our patient, it is possible that the renal disease in his case is connected with the tonsillar infection, and that the recent acute attack of tonsillitis increased damage originally done, and for the first time brought about distinct renal symptoms.

In the matter of the treatment of renal disease, what is your idea of the diet that is appropriate?

MR. A.: I think that the diet should be restricted in the matter of protein foods, and should contain as little as possible of irritating substances of all kinds. The total amount of diet should be rather restricted.

DR. STENGEL: What is the purpose of restricting the protein foods, and what do you mean specifically by these?

MR. A.: Protein foods are restricted because the nitrogenous end-products such as urea, uric acid, creatinin, etc., are excreted through the kidney, and presumably, if in excess, may further irritate the already damaged organ. Also, when the kidney is damaged, and its power to excrete nitrogenous end-products is reduced, the taking of too much protein food would lead to accumulation in the blood of nitrogenous bodies.

DR. STENGEL: What, as a practical matter, would you regard as proper directions to give your patient?

MR. A.: I would exclude all red meats and reduce meat foods generally.

DR. STENGEL: So far as red meats are concerned, the restriction of this probably is not very much more desirable than the restriction of other meats; possibly the presence of certain extractives may make a difference, but it has done more harm than good that attention has been so fixed upon the red meats. It has led laymen and even physicians to believe that other forms of meat might be eaten indiscriminately. As to the degree of restriction, we must bear in mind that a certain amount of

albuminous food is necessary in the nutrition of the body, and that excessive restriction accomplishes no useful purpose—rather, the reverse. If the total amount of protein food in the form of meat, eggs, milk, and the vegetables containing protein is kept at or below 50 grams per day sufficient restriction will be practised.

As to other irritating articles of food which you referred to, I think there is no doubt that various condiments and like foods are to be used with some care.

It is undesirable, however, that a patient suffering from renal disease should be starved. The amount of carbohydrate and fat food should make up for restriction in protein, so that his total caloric supply is not too greatly impaired.

What effect on the progress of the disease would such dietary regulation have?

MR. A.: I presume that by relieving any further irritation of the kidneys from the taking of improper food, the disease would have a better chance to subside.

DR. STENGEL: Are there any remedies which would help in furthering this desirable end?

MR. A.: I think that various diuretics and purgatives are given where dropsy or uremic symptoms occur.

DR. STENGEL: But, leaving out of consideration the complicating symptoms, what have you to say about remedies that would have a direct effect upon kidney disease?

MR. A.: So far as I understand there are no remedies that can improve the damaged kidney cells themselves.

DR. STENGEL: This I think is a fair statement of the facts. Perhaps it may be well to discuss for a moment the use of iron in the form of Basham's mixture. You will find the administration of this preparation a very wide-spread practice among physicians, and I therefore want to say a few words about it. Undoubtedly, Basham's mixture is a mild diuretic and may, in some circumstances, serve a useful purpose on this account. Moreover, in anemic cases the iron in the preparation may prove useful; but in general the practice of administering Basham's mixture seems to me very largely based upon the feeling

that some sort of drug treatment is called for in every disease; an error that is at least as great and far more prevalent than the other error, that drug treatments are never advisable. Fortunately, people are becoming sufficiently informed regarding disease and its treatment that it is no longer necessary to use placebos to retain their confidence. In the occasional case when a placebo is necessary for this purpose, and to make prolonged conversation unnecessary, we should make sure that the one selected is entirely harmless. You will gather, and I do not wish altogether to deny the correctness of your suspicion, that in my judgment Basham's mixture in the treatment of nephritis falls in the category of placebos.

Let me go a step further in this matter of drug treatments. I seriously question whether we are not too much inclined to resort to active measures for the relief of such symptoms as dropsy. The practice of purging or sweating dropsical patients violently or of using strong diuretics may quite possibly do harm to the patients without influencing the disease in any favorable manner. Merely to remove dropsy does not necessarily help the diseased kidney. Judgment must be used here as in all our therapeutic efforts. When dropsy is doing mechanical harm it must be dealt with vigorously; otherwise it may be treated by more moderate means.

If dietary restrictions and general regulation of the patient's hygiene have been attended to, there remains only the matter of removing any further possibilities of repetition of the same sort of attack on the kidney integrity as initiated the trouble. Let us take our case as an illustration. If it is true that the kidney disease in this young man resulted from tonsillar infection, and he is subjected to repetitions of this infection, a removal of the local focus gives the best chance of relief from the disease. Of course, in the presence of dropsy or other complications, one might well hesitate to undertake operative intervention, but after suitable preliminary treatment I think we might very properly discuss this.

Let me now, very briefly, refer to a patient whose case is very much in point with our discussion. As the after-result in this

patient is known, the possibility of fundamentally relieving cases of fairly advanced chronic nephritis by removing foci of infection is quite definitely shown.

Mr. X, aged fifty-five, an attorney, came under my care on account of generalized pains affecting his limbs, and a very severe pain in his back, and extending around the lower part of the right chest. The history was as follows: He had been in his usual health up to the Fall of the year, when he was first taken ill. At that time he had an attack of boils or small carbuncles at the back of his neck, which eventually required incisions, and were somewhat slow in healing. In six weeks, however, he was quite relieved of this, and, though a little weak, thought himself quite well. In February of the following year, while walking on the street on a somewhat inclement day, he was suddenly seized with a sharp pain in the right side of the back, about the level of the fifth dorsal vertebra. This was so severe that he was compelled to return home and go to bed. His physician thought he had pleurisy, but no very definite signs were discovered. From this time onward his symptoms became more generalized, though the pain in his back remained persistent, and as time went on radiated about the lower portion of the right chest. After some time the pains in his limbs set in. These were never sharply localized in the joints, but seemed diffuse throughout the whole limb. The smaller joints, however, of the hand were somewhat tender and slightly swollen. The patient's general health was more and more impaired. He lost flesh, grew pallid, and from time to time had slight elevations of temperature, but never very much, and never continuous fever. When he first came under my observation he was bed-ridden, and presented the symptoms I have outlined. There was a slight degree of pitting on pressure over his tibia and the dorsum of his feet; the face also seemed a little puffy. He was very pale, and examination of his blood showed 3,500,000 red corpuscles, 9000 leukocytes, 55 per cent. of hemoglobin. The urine had been repeatedly examined from the beginning and showed a specific gravity varying from 1010 to 1017. There was constantly a

cloud of albumin and many casts, hyaline, light and dark granular, and sometimes with a leukocyte or epithelial cell on the surface. The amount of urine was scanty. Blood-pressure was from 150 to 160 systolic, 80 to 90 diastolic.

The condition of the patient's mouth was very bad. The teeth were all loose, and pus exuded from the gums at the neck of the teeth. Some of the molars were missing. The throat was negative. Heart and lungs and abdominal examination negative. There was tenderness over his spine at the level where he had had pain, but there was no swelling. *x*-Ray examination of the teeth showed very bad conditions of the root-sockets. After some little preliminary treatment without much avail it was decided to remove the diseased teeth, and all of them were extracted at one sitting. There was a slight rise of temperature after this for a day or two, and then the temperature became normal and the gums healed very promptly. A temporary, and later a permanent, set of artificial teeth were provided. This was done as quickly as possible so as to gain time for improving the general nutrition. The patient remained for a month or six weeks in the hospital and gained very noticeably—almost from day to day. His color returned and with it his flesh and customary strength. Shortly after the removal of the teeth the condition of the urine cleared up; the albumin and casts diminished and then disappeared. After some months there was a complete restoration of the patient's health, and he was able to return to a very active practice. In this patient, besides the urinary findings indicative of renal disease, there was also marked anemia and arthritic symptoms suggestive of a rather bad focal infection. The nephritic phenomena were never marked, but were sufficiently pronounced to have occasioned considerable apprehension on their own account, and also gave rise to the belief that an underlying chronic nephritis was the basis of all the other difficulties. Instead, as you see from the result, the renal disease was but one of the consequences of a chronic infection and readily disappeared when the source of infection was removed.

I have here referred to but one case at present awaiting further treatment, and one that has been relieved by surgical measures, but I might readily have given you a number of similar instances. In particular, I have had under my care several instances in which removal of diseased tonsils was followed by most satisfactory clearing up of all evidences of an existing nephritis.

CLINIC OF DR. HOBART AMORY HARE

JEFFERSON HOSPITAL

CARDIAC DISEASE AND DIGITALIS

I THINK it may be said without fear of contradiction that there is no drug more abused, both as to the type of case to which it is administered and in the doses which are given, than digitalis. In the first place, it would seem that a goodly number of men still give digitalis in valvular disease of the heart as if they were under the impression that the valvular lesion could be healed by this drug. How such an error gained so wide a vogue is difficult to conceive, since any one who has ever seen diseased cardiac valves in autopsy must have been impressed with the fact that no drug like digitalis could produce any change for the better in their condition, but rather that if too freely used it might increase the stress and strain placed upon diseased valves, or, by reason of this stress and strain, cause colonies of micro-organisms or masses of fibrin to be swept off into the circulation and then to be lodged in distant parts where the results are disastrous, according to the importance of the point of lodgment.

Possibly, because this delusion in regard to the effect of digitalis has been so wide-spread, the drug is sometimes given as soon as a murmur is discovered, or, if the murmur is a loud one, its very loudness is thought to be an evidence of advanced disease which digitalis may remedy, when, as a matter of fact, in practically all cases, the very loudness of the murmur is a sign that the heart muscle is not fatigued as the result of its efforts to compensate for the valvular lesion, and that it is sufficiently strong to drive the blood so vigorously that a loud murmur is produced. It happens, not infrequently,

that patients with valvular disease, associated with fatigue or exhaustion of the cardiac muscle, present themselves, and, no murmur being heard, the possibility of a valvular lesion being responsible for the conditions present is dismissed. Some days later if, under rest the tone of the heart muscle improves, or if by chance digitalis has been used, the physician finds a murmur, and then wakes up to the fact that previously the heart muscle had been too feeble to engender one. It is, therefore, not out of place at this moment to emphasize the fact that before the physician is willing to express an opinion to the patient, his friends, or to himself, as to the exact condition which is present, he should examine the patient more than once, and at least one of these examinations should be after the patient has been in bed at rest for at least twenty-four to forty-eight hours or even longer.

In some cases rest is all the treatment that the tired heart muscle needs; in all instances it is certainly the most important part of the treatment, and any good that digitalis may have the power to accomplish is to be regarded as of secondary importance. To give digitalis to a patient with a failing heart and permit him to go on with his business is like stimulating an exhausted horse at the end of a long drive and, then, continuing to drive, instead of putting him in a stall and providing him with rest and good food.

This habit of giving digitalis and permitting the patient to go about is not only disadvantageous for the patient, but disadvantageous for the doctor, in that it produces a condition in which it is impossible for him to determine exactly how much digitalis the patient's heart really needs to improve its nutrition and regulate its mechanism. To use another simile, it is no more sensible than attempting to determine the cause of lameness in a horse when he is going at full speed on the racetrack instead of examining him and treating him in the stable. Doses of digitalis which are quite adequate for the patient's needs when he is resting are either inadequate when he is exercising, or the effect of exercise, combined with the effect of digitalis upon the cardiac mechan-

ism, produces a condition which is more abnormal than before the drug was given.

Comparatively recent investigations by physiologists and by clinical physiologists have, of course, thrown a flood of light upon the cardiac mechanism and have served to emphasize the fact that not only is digitalis useless for the valvular lesions, which we have known for years, but that in certain cases of ruptured compensation or faulty cardiac action its administration may not only be useless, but actually result in the death of the patient.

It will be recalled that the school of physiologists which has advocated the so-called neurogenic theory of cardiac action are now in the hopeless minority, and that the myogenic theory has been practically universally accepted. The peculiarity of this theory is that, entirely apart from the nervous mechanism, the heart muscle has the ability to originate its own contractions. The impulse for these in the healthy heart is given off by the primitive bundle of tissue at the sino-auricular node, and passes over the wall of the auricle and then to the ventricle, across the auriculoventricular junction, by means of His' bundle, which, bifurcating, as does the trachea, is divided up into many subdivisions of muscular fiber over which the contraction impulse is distributed to the ventricle wall. For the carrying out of a contraction in a normal manner it is, therefore, essential that four functions shall be adequately performed: the origination of the impulse, its transmission by virtue of normal conductivity, the maintenance of normal irritability, so that when the impulse arrives the muscle will act, and, last of all, by the maintenance of normal contractility, so that a full response, resulting in the adequate propulsion of blood, will occur. Now, it has been known for many years that digitalis increases the power or contractility of the heart, and it has also been known that simultaneously it diminishes the cardiac rate by stimulating the vagus nerves centrically and peripherally. For this reason a heart subjected to the action of digitalis may in one sense be said to be subjected to two opposing influences, one of which urges it on to increased endeavor, while the vagus influence tends to retard

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it, and oftentimes these opposing influences, when the dose of digitalis is excessive and particularly if the heart is subjected to any strain, causes an extraordinary degree of irregularity and abnormal function. So powerful are these influences that it is quite possible to produce abnormalities of heart action in an otherwise healthy heart by the administration of overdoses of this drug; or, to express it differently, such abnormalities in cardiac action of a very diverse character can be produced by digitalis that a state practically identical with disease may be temporarily, and possibly even permanently, induced. This serves to emphasize the point, already emphasized, that digitalis, like all other drugs, sufficiently powerful to do good when rightly employed, is also sufficiently powerful to do serious harm if wrongly employed.

There is not time in this lecture to consider in full detail all the problems associated with disordered cardiac functions and their relations to digitalis, nor is there time to discuss the methods by which digitalis not only acts as a cardiac stimulant, but also increases the nutrition of the heart muscle through the improved circulation in its own vascular spaces and by increasing the period of rest between beats during which time its irritability, conductivity, and contractility are adequately restored. The very slowing of the heart which digitalis induces, when used in proper dose under proper circumstances, enables the heart to do better work on one-half the number of beats per minute, without exhausting itself, than it was doing on a high number of beats per minute and rapidly playing itself out. How often do we see cases in which the rapid action of the heart is the only symptom which strikes us as of evil import, its presence indicating that, even if the patient may be doing well at the moment, the heart muscle cannot maintain that pace for many hours without disaster.

In mitral regurgitation, with ruptured compensation arising chiefly from cardiac fatigue, digitalis, in proper dose, is, of course, useful, provided rest is given. The rest of the body and the slowing of the heart by the drug may soon restore cardiac function, and the drug, if properly used, is safe if there is no lesion

of the heart muscle, the evil results of which will be emphasized by its physiologic action. In some instances the history is that the patient, receiving large doses of digitalis, is at first improved wonderfully, and then, within a short space of time, the last state of that man is worse than the first, probably because the large doses which were needful in the beginning have been continued until, through the prolonged effect of each individual dose, a cumulative influence has induced a digitalis poisoning of the heart, although the individual doses may not in themselves be poisonous.

It is in connection with lesions usually associated with mitral stenosis that digitalis is to be used with the greatest caution, or not at all, and it is in connection with these lesions that digitalis may, on the one hand, be life saving or death dealing. If the problem is simply one of obstruction at the mitral orifice, the increased driving power given to the right ventricle by the digitalis pushes the blood through the obstructed orifice more completely, and the slowing of the ventricle gives more time for it to be adequately filled from the auricle. If, however, as is the case in many instances, the lesion is not only a narrowing or obstruction of the orifice, but consists in an erosion and partial or complete destruction of the fibers of His' bundle, then digitalis may do great harm, for the disease, by interfering with the passage of the impulse from the auricle to the ventricle, may induce a partial heart-block, and when digitalis is given, this drug, by stimulating the vagus, makes it more difficult for the remaining fibers of His' bundle to perform their function, with the result that a partial heart-block is changed into a complete heart-block. This is the more true, as it would seem probable that digitalis, apart from any influence on the vagus, directly diminishes the conductive power of His' bundle. This may result in sudden death or a great exaggeration of cardiac distress. Unfortunately for the practitioner, it may be difficult or impossible to determine the presence of partial heart-block without the use of the polygraph. On the other hand, if the heart-block is complete, as the result of total destruction of His' bundle and the patient has survived the onset of complete heart-block, as he often does, there is now

a condition developed in which the ventricular wall, finding itself deprived of its normal impulse to contraction, begins to originate its own impulses and saves its life by calling in this substitute mechanism. As a rule, this substitute mechanism results in an exceedingly slow heart-rate, and the complete block in His' bundle, having practically cut off the inhibitory restraining influence of the vagus nerves, which act chiefly on the auricle or upon His' bundle, the digitalis is free to act as a direct stimulant to the heart muscle, and the result is that the ventricle beats more rapidly and approaches its normal rate. The danger of excessive doses of digitalis in this condition is, therefore, not to be overlooked, since the ventricle, being deprived of indirect vagus influence, may be stimulated into excessive systole and rapidly exhausted by the action of the drug. Many cases of sudden death in patients suffering from cardiac disease, who have at first greatly improved under treatment, are explained by the recognition of the importance of a lesion in His' bundle and the action of digitalis upon it.

Time permits me only to discuss one more important cardiac condition in which the digitalis, properly used, produces very beneficial results, namely, in so-called auricular fibrillation. Not because it is able apparently to correct fibrillation, which probably always continues, but because by its decrease of the conductivity of His' bundle it prevents the ventricle from being started off into contraction so frequently that its beat is inadequate and its period of rest is cut down to almost nothing. It also does good in these cases by stimulating the right ventricle, so that the blood is delivered into the fibrillating auricle with sufficient *vis a tergo* to make a better delivery of blood through the left auricular-ventricular opening into the left ventricle. In some cases it is possible only by means of the polygraph to determine whether full doses of digitalis are to be used to put aside the evil effects of fibrillation or whether they are to be absolutely tabooed lest they induce heart-block.

Last of all, let me say a word in regard to myocardial degeneration and the use of digitalis. Physicians are too prone to forget the teachings of pathology and of the postmortem room.

If they are not optimists they probably will not be successful practitioners, but optimism must not go so far as to make a man blind as to possibilities. The physician, therefore, who in a case of failing heart administers digitalis in what he thinks to be suitable doses and fails to get results must not feel pessimistic as to the value of digitalis. In cases of cardiac failure we must recognize that if the heart muscle is degenerated and its fibers segmented neither digitalis nor anything else will restore it to normal functional activity. Sometimes the underlying cause of myocardial degeneration may be renal disease or the causes which induce renal disease. It originates in the course of the acute infections, in which case digitalis, as a cardiac stimulant, often fails, to our great disappointment, for reasons which are obvious when we stop to think about them, or the condition arises as the result of syphilis, metallic poisoning, or the result of age superimposed upon partial degeneration originally induced by some acute infection like rheumatism, influenza, typhoid fever, or diphtheria. Digitalis deserves no reproach when it fails in many of these cases, for it always will and must fail until some drug is found which can develop new tissue for old, and when such a drug is found, to use a biblical expression, "there will be no sorrow, neither will there be any more pain," and, possibly, I may add, neither will there be death!

When digitalis fails to do good, provided that an active preparation is employed, such as a physiologically tested tincture or digitalone, which, in concentrated form, represents all the active ingredients of the leaf, and good results fail to accrue, the condition which is present makes its normal physiologic action impossible, or the physician has made a mistake in diagnosis or dose.

CLINIC OF DR. JOSEPH SAILER

PHILADELPHIA GENERAL HOSPITAL

AORTIC ANEURYSM[1]

History; Physical Findings; Their Discussion; Pulselessness With a Maintained Circulation; Explanation of This Phenomenon; Prognosis; Treatment; Autopsy.

THE first patient I shall bring before you today is a negro forty years of age. His occupation has been that of a hod-carrier. The history can be discussed very briefly. As far as he knows his family and previous history are both unimportant. He denies venereal disease or any other serious illness. Two months ago he felt pain in the chest, began to be short of breath and to have a severe cough; complaints that, as you are aware, are exceedingly common in this institution. On the 10th of March he was obliged to stop work, and since then all his symptoms have been growing steadily worse.

It is very obvious that the man is desperately ill. He has persistent orthopnea and cannot either lie down or stand up, a fact that is annoying to my colleague in the *x*-ray department. Orthopnea, as you know, occurs in many conditions—cardiac disease, asthma, bilateral pleural effusion, acute pneumothorax, tumors of the mediastinum, etc. In the present instance a discussion of this subject would not be profitable because there are other features of the case that yield more definite information.

As I expose the upper portion of the body you will observe that the left arm is greatly swollen. He does not appear to be paralyzed, for you see he can move it easily, the swelling pits

[1] Clinic delivered before Fourth Year Class of the University of Pennsylvania at the Philadelphia Hospital, May 11, 1917.

readily and deeply on pressure, and as I press the arm there is no sign of tenderness nor does he hold it as if it were painful. The right arm is normal. You can see, further, that the veins over the upper portion of the chest on the left side are greatly distended, forming a network upon the skin, and as I test them you will further observe that the current of the blood is from the shoulder toward the sternum. Swelling of one arm occurs in a considerable variety of conditions. We find it in local inflammations of the arm, such as cellulitis, phlebitis, and injury. In these conditions the arm is usually tender as well as painful. It occurs in neuritis as a very obstinate painful condition associated with exquisite tenderness. It occurs occasionally as a result of the development of secondary carcinoma in the lung and chest after a breast amputation, and it is also observed as a result of mediastinal tumor if it compresses the subclavian or innominate vein on one side. It is occasionally seen as a result of the swelling of the axillary lymph-nodes and of malignant tumors of the arm or shoulder.

Now in this case we can exclude inflammation because the patient's temperature is normal and there is no tenderness. The latter fact also excludes injuries and neuritis. Secondary carcinoma is too unlikely for us to linger upon it as a cause and the axillary lymph-nodes are not enlarged. We are, therefore, justified in suspecting a mediastinal tumor. This suspicion is rendered almost certain by the fact that the superficial veins in the left chest are distended. As the veins in the neck are not distended we can conclude that it is not the innominate but the left subclavain vein that is compressed.

Now, by all odds, the commonest mediastinal tumor is an aneurysm of the aorta. We therefore suspect this, and direct our investigations to its exclusion or proof. The upper portion of the left chest is dull, but no matter how carefully we examine it we fail to find either pulsation or thrill, and on auscultation there is no evidence of a bruit. The apex-beat is in the fifth interspace, slightly inside the midclavicular line. All the heart sounds are clear. There is no murmur and no accentuation of the second aortic sound. As I place my two fingers under the

cricoid cartilage and lift gently I feel a distinct tug that resembles nothing so much as the nibbling of a fish on the line. The harder I press upward, the more distinct it becomes. This symptom was described by Oliver in 1888 as a pathognomonic sign of aneurysm. It is not so much a sign of aneurysm itself as of the adhesions produced by the growth of the aneurysm; that is, it is a sign of that mediastinitis or mediastinal adhesions that practically always accompany thoracic aneurysm. Therefore, tracheal tug may be used as one of the definite and practically positive signs of aneurysm. The lungs except the left upper portion, where there is dulness, faint breath sounds, faint vocal resonance, give the normal resonant note and at their bases move freely. On auscultation, the respirations are vesicular, but there are numerous loud râles of a tracheal or bronchial type. The pupils are equal and react freely to light. We may, therefore, conclude that our aneurysm, if there is one, does not compress the sympathetic nerve on the left side. The patient, as you have noted, has coughed several times during the examination. The cough is of a dry, harsh character, described, for some reason that is not quite clear to me, as "brassy" in character. I feel quite sure that the laryngologist will find disturbance of the left vocal cord due to the left recurrent laryngeal nerve, which has been involved and injured by the aneurysm.

If we attempt to aid our diagnosis by a consideration of the pulses on the two sides we find something very extraordinary. The patient is entirely pulseless. Neither in the radials, carotids, femorals, posterior tibials, or dorsales pedes arteries can we detect any pulsation whatever. When the man came in, curiously enough, the left radial pulse could still be felt, but the right was not palpable. This in spite of the fact that the left subclavian vein was compressed. When I first examined him two days ago no pulse could be detected anywhere.[1]

A good many years ago François Frank, of Paris, who, with Marey, used various graphic methods for recording the pulse-wave, observed that sometimes in aneurysm a peripheral pulse

[1] There is apparently no term for this condition. I venture to suggest "pulsus deletus."

could not be felt. He ascribed this to retardation; that is to say, to a delay in the transmission of the wave. He was able in one case to detect, nevertheless, that there was a certain rhythmic distention and collapse of the blood-vessels by the ingenious method of placing the patient's hand in a cylinder filled with water, and then recording the increase in the bulk of the whole hand and its collapse synchronous with the pulse.

We are not able in this case to do this experiment. I do not doubt, however, that if it could be done we might detect as much of a pulse relic as François Frank observed.

François Frank made some other observations that are of considerable interest. Extreme retardation of the pulse leading to inability to palpate it occurs, he said, only in aneurysm. It never occurs, however, if, in addition to the aneurysm, aortic insufficiency is present, and you know that the two lesions not infrequently occur together. I shall endeavor in a few minutes to explain why this statement is probably correct.

Austin Flint also observed loss of pulse in aneurysm, as have doubtless many others, although I have not studied the literature very thoroughly. He was not impressed, however, by the fact that the circulation is maintained in the pulseless part, and assumed, as I believe incorrectly, that the loss of the pulse was due to the compression of the artery. Hirschfelder also speaks of this retardation, but whether he is merely quoting Frank or has made some observations of his own is not clear from the text. This phenomenon has interested me very much. This is the third case in which I have been able to observe the absence of the pulse and the persistence of the circulation.

The first was a man brought to my office by his two physicians, who supposed that he was suffering from some strange form of myocarditis because they could not detect the radial pulse on either side. There was, however, a faint pulse in the dorsales pedes arteries. The patient was suffering from only a mild dyspnea. He had some pain in the thorax. The hands were warm and blood flowed freely when the finger was pricked. It was not difficult to elicit signs of aneurysm of the arch of the aorta, which were confirmed almost immediately by the *x*-ray

picture. This was before the days of the Wassermann, so that syphilis, although suspected, could not be determined. The man died shortly afterward, but no autopsy was obtained.

The second case was a patient in my ward in this hospital. The pulse was lost only in the right radial artery, but again I was able to demonstrate all the signs of persistent circulation in the right arm. The patient passed from observation and no autopsy was obtained.

How can we explain this phenomenon? It seems to me that a perfectly satisfactory explanation can be given by comparing the aneurysm to the elastic rubber bag that forms a part of the air-pumping system that is used with several forms of apparatus, such as the Paquelin cautery. In this system we have a pumping-bag supplied with valves and a soft rubber bag without valves, usually enclosed in a net to prevent its rupture. Each time the hand compresses the pump a jet of air is thrown into the elastic rubber bag until it is distended. After it is distended each time that the pump is compressed there is a slight expansion of the bag, but its persistent elasticity maintains through the outlet tube an almost continuous current of air. Let us suppose that the aneurysm acts in the same way, that with each contraction of the left ventricle it is slightly distended, but that its elasticity maintains an almost continuous current of blood flowing through the peripheral circulation. If we had the apparatus used by François Frank it is entirely possible that we would be able to obtain tracing that would resemble the long blunt waves that he pictured, but with the finger it is quite impossible to detect any pulsation. I assume without hesitation that this is the state of affairs in the present case, and this assumption enables us to reach a fairly definite conclusion regarding the location and character of the aneurysm. In the first place, it must begin between the heart and the origin of the innominate and extend beyond the origin of the left subclavian. It must be a fusiform aneurysm, because a saccular aneurysm would not absorb the pulsations in the way that occurs in this case. The wall must be still fairly elastic, and the aneurysm probably contains only a moderate number of clots, because otherwise the postulated

conditions would not be fulfilled. Because he has a very active tracheal tug we add mediastinitis to our diagnosis, believing that adhesions have formed between the aneurysm and the surrounding structures, and we assume further that the aneurysm has extended far enough to the left to compress the left subclavian vein. It extends far enough posteriorly to compress the trachea, and it is this compression more than any other factor, I believe, that is accountable for the orthopnea.

I said that I would endeavor to explain why the pulse did not show this retardation or disappearance in those cases in which the aortic valves are incompetent. It may be assumed that the very high pulse-wave of aortic insufficiency cannot be completely obliterated by the aneurysmal sac, at least an aneurysmal sac that is likely to occur in human beings, and, therefore, at least a certain amount of pulse will always remain perceptible in the peripheral arteries. I admit that this is, to a certain extent, begging the question, but I do not know how any definite knowledge is to be acquired on this subject unless someone should have the opportunity of observing cases of this kind during the pulseless period and subsequently after the development of aortic insufficiency. If any such observation has ever been made it has, I am sure, not been recorded.

Let me say just a few words about the aneurysm of the thoracic aorta. It is by far the commonest aneurysm, forming about one-third of all the aneurysms that are observed. It is particularly a disease of males. Of all the thoracic aneurysms, more than nine-tenths occur in this sex. It may be regarded practically as a syphilitic disease. The number of cases that are supposed to be not syphilitic diminish, with improved methods of investigation, to the vanishing point.

Let me speak now of the two features that in every case most nearly interest the patients themselves. These are prognosis and treatment. The former may be dismissed very briefly. The prospect of recovery in this case does not exist. Neither nature nor art knows of any remedy that will cure a thoracic aneurysm. The prognosis for the duration of life is also exceedingly unfavorable. This aneurysm has attained a large size, has

formed numerous adhesions, and is exerting pressure upon at least one vital structure, the trachea. There is no hope, therefore, that we shall be able to modify its course in such a way as to afford the patient more than temporary relief. Life is a matter of days. I do not believe that he can continue to live as long as a week.

TREATMENT

The question of treatment, therefore, in the present instance is not important, although it may not be amiss to call attention to some of the methods that have been used in the past for relief of this condition. In the olden days our surgical colleagues were busy with their ligatures. I can remember, as a student, seeing cases in which the carotid and subclavian arteries had been ligated in an effort to control a thoracic aneurysm. This in spite of the fact that the true nature of aneurysm had been repeatedly stated, and it was reasonably sure that the syphilitic process would continue in spite of the ligatures and render them useless. Later, when it was seen that the natural process was the deposition of laminated clots, diet and rest were employed. It is doubtful whether the diet had much effect, but the rest was certainly beneficial. Tufnell did more than any other to standardize this treatment. Still later calcium and, particularly, gelatin were used to increase the coagulating time of the blood. The latter was injected hypodermically. I have tried this treatment in several instances and I cannot say with encouraging results. Still later further effort was made to promote clotting by introducing wire into the aneurysm. This has been practised particularly in this country by Dr. Hare of Jefferson College. I have used it in a number of instances, and in favorable cases I know few methods of treatment that give such immediate brilliant results. An aneurysm apparently can be reduced to a small hard lump barely palpable by the introduction of a few yards of wire. I had hoped to have a suitable case this winter on which the operation could be performed before the class, but nothing has presented. A fusiform aneurysm, of course, is not available. A saccular aneurysm, however, lends itself readily

to this procedure. The hollow needle coated with porcelain is introduced into the aneurysm, and through this is fed from 20 to 40 feet of some soft plastic wire, preferably gold wire, very slowly and carefully, to avoid kinking, and then the end of the wire is attached to an electric battery and a current of electricity passed through it. This is the most important and most delicate part of the whole operation. A large pad is placed over the patient's back, to which the negative pole is attached, and the positive pole is attached to the wire. Five milliamperes are passed for about five minutes. Then in successive stages the current is increased 5 milliamperes at a time until about 40 milliamperes have been reached. If there should be any burning or any other subjective sensation, this is reduced. It requires from one-half to three-quarters of an hour properly to make the electric application. It must not be hurried and the increase must be made by someone who is reasonably conversant with the use of the galvanic battery. At the end of this time the end of the wire is cut off. It is then pushed through the needle and beyond its point by a plunger, the needle withdrawn, and a light dressing applied over the wound. The change in character of the aneurysm from a soft, violently pulsating sac to a hard nodule occurs during the operation. I have never had any unfavorable accident while doing this. On one occasion, however, in wiring a saccular aneurysm springing from the ascending portion of the arch of the aorta an *x*-ray, taken a few days afterward, showed that a loop of wire had slipped through the aortic orifice and had entered the left ventricle. I was much alarmed, but, as the subsequent history showed, quite needlessly. The loop remained in the heart, where, apparently, it never produced any symptoms whatever, and the man passed from observation some months later apparently quite well.

The wiring alone is merely a temporary expedient. We must endeavor if possible to control the syphilitic process, and for this the ordinary methods of treatment should be employed. In the present instance we are giving this man some mercury and iodid, but with an unconquerable feeling of pessimism that should be foreign to the therapeutist.

NOTE.—The patient died one day after the clinic. Permission to perform an autopsy was refused by the family, but my resident, Dr. Schaar, who is enthusiastic and persistent, went to his home and finally persuaded them to let him make a partial autopsy while the body was in the coffin and after embalming had been done.

The thoracic cavity only was opened. The following are Dr. Schaar's notes:

The pleuræ on both sides were thick and adherent. The adhesions were very dense and the pericardium was adherent to the surrounding structures, but there were no adhesions of the two layers of pericardium. The heart showed no signs of hypertrophy or dilatation. The left lung was removed, but did not show any sign of consolidation or cavity formation. The right lung was not removed, but no pathologic changes could be made out by the sense of touch. The mediastinum appears to be a mass of dense adhesions. At the upper part and slightly to the left was a tumor the size of a large orange. On removal this proved to be an aneurysm beginning about 2 cm. from the semilunar valves and including the ascending, transverse, and part of the descending aorta. The aneurysm was lined with a laminated fibrinous deposit.

LEUKEMIA

History; Physical Findings; Blood Picture; Discussion of Etiologic Theories; Associated Symptoms; Prognosis; Treatment; Arsenic; Benzol; *x*-Ray; Radium; Splenectomy.

THE second case that I desire to present today I have borrowed from the wards of Dr. Piersol. He is a white boy, eighteen years of age, born in this state, and by occupation a laborer. He was admitted to the hospital complaining of a lump in the left upper quadrant of the abdomen. Briefly, the history is this: About December 7th he caught cold. He felt dizzy at this time and had chilly sensations. On the 10th of December a lump was noted in the region of the umbilicus and appeared to extend to the left side. A month later he had a sore throat, cough, and expectorated a semipurulent sputum. The lump very rapidly increased in size, and soon extended to the crest of the ileum and completely filled the left half of the abdomen. There was some epistaxis, but apparently otherwise no bleeding. The family history is negative. At the age of eight years he had measles and has had repeated attacks of tonsillitis. His habits are stated to be good, although he uses tobacco to excess. He has done various kinds of outdoor laboring work. With the physical examination, as the time is short, we need not detain ourselves long. We find slight prolongation of expiration, but no râles in the chest. A systolic murmur is heard over the whole heart, most loudly at the base. The pulmonic second sound is moderately accentuated. As I expose the abdomen you see that the left side is distinctly distended. As I press upon it you will observe that this distention is caused by a solid mass. As I percuss there is absolute flatness. By bimanual palpation you can observe that the hand placed in the flank lifts the tumor and with it the overlying palpating hand. It therefore fills up the whole of the left side of the abdomen. Its surface is smooth. As I trace its outline you can observe that its right edge leaves the costal

margin at the right border of the sternum, extends obliquely downward and toward the right, and is about 2 cm. to the right of the umbilicus. It then extends downward and to the left, and curves transversely until at its lowest point it is about 2 cm. beneath the anterior superior spine of the left iliac bone. Just above the umbilicus can be felt a very deep notch. You will observe that as the man breathes this tumor moves with respiration.

We have no hesitation, therefore, in regarding it as an excessively enlarged spleen. There are not many conditions that give rise to a spleen as large as this—chronic malaria, Banti's disease; possibly, in its extreme type, amyloid disease, polycythemia, and leukemia. You will remember also the small colored boy whom I showed you earlier in the year, and who had a spleen relatively almost as large as this, and whom we decided was suffering from von Jaksch's type of anemia, chiefly because there was a persistent mild leukocytosis.

In all these conditions the examination of the blood is decisive. In Banti's disease there is a leukopenia with an increase in the lymphocytes, in polycythemia a great excess of red cells, in von Jaksch's disease anemia and leukocytosis, and in leukemia an enormous increase in the white cells. I will, therefore, turn to the blood report in this case. On the 9th: hemoglobin, 28 per cent.; red blood-cells, 1,300,000; white blood-cells, 700,000. This is only his second day in the hospital and more extensive studies will be made, but it is sufficient for the purpose of diagnosis. The differential count showed:

Polymorphonuclears	22 per cent.	154,000
Lymphocytes	10 "	70,000
Eosinophils	1 "	7,000
Basophils	9 "	63,000
Large lymphocytes	2 "	14,000
Neutrophilic myelocytes	44 "	308,000
Eosinophilic myelocytes	12 "	84,000

Many nucleated red blood-cells.

We have, therefore, before us a case of myelogenous, myeloid, or chronic leukemia. We do not know the cause of leukemia.

There have been various suppositions—one that it is an infection, another that it is a liquid malignant tumor, which is no explanation because we do not know what malignant tumors are; another that it is a disturbance of the blood-making and destroying organs, but as the nature of this disturbance is not stated this gives us no clear conception of the disease. As for the nature of the disease, that is reasonably clear. Either there is an excessive production of white blood-cells, or a deficient destruction, or a combination of both processes. In favor of the former is the appearance of abnormal cells; in favor of the latter I have regarded the extreme fragility of the white cells, which you will note when I speak of the results of certain forms of treatment. So rapidly are vast numbers destroyed without injury to the other tissues that it seems as if they invited destruction. The subject admits of much discussion, but no solution. What becomes of the white cells after their therapeutic destruction is a mystery. The non-coagulable blood nitrogen is low in leukemia and remains low during treatment, a fact that seems to be against leukocytosis. We find in the blood this great excess of white blood-cells, including the presence of a large number of cells that are not found under normal conditions, the so-called myelocytes. The red blood-cells present the picture of a severe, even a pernicious, anemia. The spleen and often the lymph-glands are greatly enlarged. The bone-marrow is altered, and we find what is called leukemia infiltration in most of the tissues.

Among the associated symptoms three are of considerable importance. They are the attacks of diarrhea, the tendency to hemorrhage, and fever. The diarrhea is usually sudden and often uncontrollable, and the hemorrhage may be sufficiently severe to threaten the life of the patient. Fever in leukemia is rather an extraordinary feature. Various types are observed, not perhaps as many as have been described by Gowers, Murchison, and more recently by others in Hodgkin's disease, but they are sufficiently numerous to exclude the idea that there is any definite febrile course. It is sometimes assumed that the rise in temperature is due to secondary infection. This may be true because there is some reason to believe that cases of leu-

kemia are more susceptible to infection than others, but in the majority of instances the infection cannot be demonstrated.

The prognosis for ultimate recovery is not good unless recent methods of treatment prove to be more efficient than those we have had in the past. The prognosis for temporary improvement in all these cases is apparently excellent, and life may sometimes be prolonged for many years.

Let me speak briefly of the treatment of these conditions. There are four remedies and possibly a fifth, although it has not been used long enough to enable us to judge of the final results.

The first is arsenic. This has been used for a long time. Ordinarily it reduces very rapidly the number of leukocytes, improves the condition of the patient's blood and general nutrition, and for a time at least there is an apparent recovery. After a longer or shorter interval there is a relapse that may or may not yield to arsenic, but even in the most favorable conditions not as completely as in the first application of the treatment, and ultimately a relapse occurs that does not yield at all, and the patient dies. I confess it does seem to me that the efficiency of the arsenic indicates the existence of a parasite belonging to the lowest form of animal life, and that possibly this parasite slowly becomes immunized to the drug, but this is the purest of suppositions.

The second form of treatment is benzol. The discovery that benzol reduced the leukocytes was an accident. The use of the drug in leukemia was recommended by Koranyi in 1912. According to Miller, in Musser and Kelly's Practical Treatment, the dose should be from 4 to 5 gm. per day. It is important to obtain chemically pure benzol. It may be given either in emulsion or in capsules, and it is sometimes desirable to mix it with olive oil. As soon as the leukocytes are reduced to 25,000 or 30,000 the treatment should be discontinued.

The third method of treatment is the *x*-ray. There are two methods, one in which the application of *x*-ray is confined to the spleen, a small area being exposed at a time, and the rest of the body being protected by a leaden diaphragm that is backed with wood to keep it from coming in contact with the skin. The

spleen is carefully mapped out and different portions treated at intervals of two or three days, sometimes daily, until the whole area has been exposed. The results of this treatment are very remarkable. The spleen shrinks in size, the leukocytes diminish in number, and it is not at all uncommon to produce a leukopenia. At the same time the red blood-cells increase. The patient gains weight and strength and is apparently well. I wish to read to you the figures that have been obtained in a case that has been under my care during the past winter. The treatments have been made by Dr. Pfahler, who was former roentgenologist to this hospital. Very briefly, a woman of about sixty years of age had a severe attack of cough in September, 1915. She gradually grew weaker, had night-sweats, and consulted a physician who discovered an excess of white blood-cells. The chart indicates the blood changes that have taken place. In addition to this, her weight has increased from 134 to 148 pounds. The spleen has shrunken, until now the lower edge can be felt only on deep inspiration beneath the left costal margin, although in the beginning its lower edge was at the level of the interspinal line and extended to the median line. She is strong and active and has no cough. The first blood count is as follows; it is not on the chart (Fig. 16):

Hemoglobin			52
Red blood-cells			2,782,000
White blood-cells			180,000
Polymorphonuclear	29	per cent.	52,200
Lymphocytes	4	"	7,200
Mononuclears	9	"	16,200
Transitionals	1	"	1,800
Eosinophils	2	"	3,600
Basophils	8	"	14,400
Myelocytes — Neutrophils	36	"	72,800
Myelocytes — Eosinophils	5	"	9,000
Myelocytes — Basophils	6	"	10,800

The other method is the application of the *x*-ray to the long bones as well as to the spleen on the assumption that the bone-marrow is primarily at fault. This, of course, is not unlikely, although it is quite possible that the change in the bone-marrow

is secondary and not primary. The results appear to be quite as good by this method as by the other.

The fourth method is the use of radium. This was described by Dr. Ordway, of Albany, who reported excellent results in one case. Dr. Giffen, of Rochester, Minn., has used this method extensively and with very remarkable results. The radium is applied only to the spleen and the application is made as it is with the *x*-ray. The protecting leaden diaphragm is of great importance in this connection. Otherwise bad burns are almost certain to occur. The effect of the radium is even more sudden and dramatic than that of the *x*-ray, probably because the rays

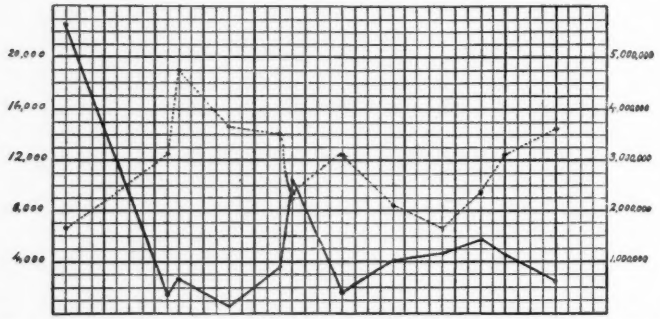

Fig. 16.—Initial count, 180,000 leukocytes. Solid black line, leukocytes. Dotted line, erythrocytes.

are more powerful and more vigorous application can be made. As these two methods are essentially the same, results may be considered together. Up to the present time permanent cure has not been achieved. As with arsenic, in time relapses occur which fail to yield to treatment, and the patient dies of exhaustion, usually hastened by the excessive diarrhea. It was in view of this ultimate failure that Dr. Giffen suggested the removal of the spleen. This has been done in several cases in Rochester, Minn., and the immediate results have been satisfactory. The remote results cannot be estimated until a longer time has elapsed. This treatment is, however, not entirely new. Warren, quoted by Osler, was able to collect 43 cases with very poor

results, and Miller, of Chicago, as a result of his studies of the literature, condemns the method as harmful. It is probable that improved surgical technic and a more careful selection of the moment of operation may yield, in time, better results. Mesothorium has also been employed, but at present the material is not available, and the scant knowledge that we have of its action does not warrant further experimentation.

CLINIC OF DR. DAVID RIESMAN

PHILADELPHIA GENERAL HOSPITAL

PROGRESSIVE MYOCARDITIS. TREATMENT OF CARDIAC DECOMPENSATION

WE have at the Philadelphia General Hospital an unusual opportunity for studying diseases of the circulation. Most of our patients are hard workers and hard drinkers, who pay the price more often with their hearts than with their livers. Many come in with symptoms of disturbed cardiac function, often of advanced degree—with dyspnea, dropsy, and serous effusions. In my early years of service I always expected to find in such patients a valvular lesion and a history of some acute infection, particularly rheumatism, but I soon learned that from the viewpoint of a previous acute infection the history was usually negative, and that physical examination often showed either no murmur at all or only a faint systolic bruit heard at the apex. On account of the presence of albumin and tube-casts in the urine such cases are often diagnosed as Bright's disease.

A special circumstance has graven one of these cases on my memory. One day, on looking through the wards for cases suitable for demonstration, I was told by my resident physician that there was a man with Bright's disease to whom he had just given a hot-pack; a good case, he thought, to show to the students.

The patient was very short of breath; he had general dropsy; no murmur of the heart; no arhythmia. Habit made me place my hand in the axilla, where, to the surprise of the intern, I was able to demonstrate a forcible apex-beat far beyond the customary area where he had looked for it. The case was one of primary myocarditis with dilatation and decompensation.

I wish there was a rule-of-thumb by which one might readily distinguish between cardiac cases with albuminuria and primary renal cases. The functional kidney test and the determination of the non-protein nitrogen or of the urea nitrogen in the blood are valuable methods, but not feasible in ordinary practice. I have always thought that a highly concentrated urine, depositing a thick, uratic sediment, is fairly good bedside evidence that the case is one of primary cardiac disease. Such urine may contain a considerable amount of albumin and hyaline and granular casts, and yet, with the establishment of free diuresis, it may clear up completely.

The pathology of these cases is not always clear, nor is it possible in every instance to square the functional disability with the autopsy findings. Sometimes the condition is one of fatty degeneration; more often it is a fibroid process, which may justify the otherwise questionable term "myocarditis." We shall, I think, eventually find that decompensation is not a purely cardiac process. It is cardiovascular or cardiovasculovisceral. Acute cardiac weakening seldom produces the clinical picture found in cases of chronic circulatory failure.

Though the heart, as I have just said, is not the only factor, it is certainly the main one, and whether the patient will recover or not depends largely upon how much sound muscle tissue remains to respond to treatment. In many cases the response is truly marvelous. In others that I would call progressive myocarditis—they almost deserve the name malignant—the course is downward, no matter what we do. I have sometimes used in consultation the expressive term "rotten myocardium," as best conveying the impression of the condition of the heart muscle that in such cases I have gotten upon examination.

In order to evaluate properly the morbid physiologic processes one must not content himself with an examination of the heart, but must look beyond, to the state of the liver, of the kidneys, of the vasomotor system (blood-pressure, pulse-pressure, etc.).

I have often longed for an indubitable sign indicating from the standpoint of prognosis the class to which a given case be-

longs, but have never found one. Only time and therapeutic failure or success can tell us. However, there is something in the color of the patients with progressive myocarditis that is almost pathognomonic. They have a sallow, pasty complexion bordering on the cachectic. I also believe that a gallop-rhythm produced by doubling of the first sound is a bad omen in chronic myocarditis with decompensation.

During the course of the disease certain symptoms may assume such striking proportions as to mislead the unwary. Let me illustrate by a case. The patient, L. P., a widower, fifty-seven years of age, had typhoid fever of a most severe type ten years ago. He is a physician with a large practice, and is accustomed, like nearly all of our self-neglecting profession, to irregular meals and insufficient sleep. His first symptoms were those of indigestion. He complained of gas and was somewhat short of breath. He had no heart murmur and the pulse was regular. So pronounced were his gastric complaints that he was for some time treated for stomach trouble, being lavaged and dieted, but without avail. When I examined him I was struck by his pasty, unhealthy complexion. He was short of breath, which he attributed to gaseous distention, and had no appetite whatever. The heart was enlarged to the left and to the right. There was no arhythmia of the pulse, but a distinct gallop-rhythm of the anapest type could be heard over the heart. The liver was enlarged; the right chest contained a small amount of free fluid; the urine was scanty, highly colored, and contained albumin and casts, and urates in great abundance. The case was one of progressive myocarditis with decompensation.

CASE II is a man about fifty-two years of age, who entered Ward 14 of the Philadelphia General Hospital with a severe cough that was thought to be due to bronchitis. His sole complaint was this harassing cough. However, when we came to examine him we found the following: He was cyanosed; there was beginning general anasarca; the heart was enlarged. There was no murmur, but a rather marked extrasystolic arhythmia. I have seen a number of cases in which cough was the most troublesome symptom—the only one the patient thought worth mentioning,

—and sometimes the only one that had received any attention from the doctor. Cough mixtures are of no avail in the cough of cardiac decompensation. Digitalis may relieve it in time, but nothing acts so well or so promptly as the hypodermic injection of morphin or heroin.

As treatment in this patient has proved very successful, I will briefly tell you what we did—the more so, as one feature inculcates a valuable lesson.

As soon as the true diagnosis had been established, we prescribed for him, in addition to the usual rest in bed and the soft diet of the hospital, a so-called Niemeyer capsule that I have used for many years. It consists of the following:

R. Pulvis digitalis,
Hydrargyri chloridi mitis,
Pulvis scillæ,
Caffeinæ, } āā 0.8.
M. et div. in capsul. no. xii
Sig.: One three times a day.

Unfortunately, through an oversight on the part of the intern, the capsule was continued for a considerable number of days, with the result that on one of my visits I found the patient horribly salivated. It took us a long time to get his mouth well, but, as you see, he seems in good health, and will soon leave the hospital cardiacally and orally in a very fair condition.

In private practice I never prescribe more than a dozen of these capsules, and tell the patient to give his mouth special care. If I find the capsules do good, and have caused no trouble, I may order another dozen. They are not equally useful in all cases of decompensation. From my experience, I should say that they do best in cases with large, congested livers, and little or no albumin in the urine, and then they often act in a truly magical manner.

In CASE No. III I want to illustrate the occurrence of mental symptoms in chronic myocarditis. Some other time I hope to talk at length upon this subject—upon the psychic state of the cardiac patient, which has never yet been exhaustively treated. For the present, however, I shall content myself with an account

of one interesting example. This is the case of Dr. R., an able physician with a widely scattered practice in West Philadelphia. He drove a motor car that had no automatic starting device and was very hard to crank. Whether it was the constant cranking of it or the usual carelessness of medical men about themselves, I do not know, but something brought him under my care with an attack of extreme auricular fibrillation with dyspnea, but without dropsy. He recovered fair compensation under rest and digitalis, but remained despondent because he was unable to resume his full practice. Gradually he relapsed into fibrillation without unusual symptoms, except his mental state. Quite abruptly he became agitated and began to shout at the top of his voice and to walk to and fro in his room like a caged lion. He kept this up for many hours without a moment's rest. His strength during this episode was marvelous. Whence it came I do not know. The attack subsided, and, to our surprise, the patient did not seem materially worse than he had been before. He eventually died from progressive failure of the circulation.

The next case illustrates a point to my mind of great diagnostic significance, which helped me in the case I mentioned at the beginning and in many others. The patient, C. A., was a man forty-two years old, always well until a few months before I saw him. He was troubled with shortness of breath, cough, and expectoration, which was at times blood tinged. There had also been some loss of flesh. When I first examined him I found a slight impairment at the right apex, and this discovery, together with the history, led me to suspect that he had tuberculosis. Such a diagnosis had, indeed, been made by another physician. When, however, I made a more careful examination, being prompted thereto by the fact that the man was easily exhausted by the slightest effort, I found that the apex of the heart was quite a distance outside of its normal position and that there was some arhythmia—both signs not common in pulmonary tuberculosis. The patient evidently had a myocarditis with dilatation of the heart; the cough was due to congestion of the lungs, to which at times were added attacks of acute pulmonary edema with expectoration of rose-colored froth. The impairment of the right apex

was probably caused by an old healed tuberculous focus. This man's myocarditis was of the malignant progressive variety—his heart never regained a proper tone; its contractions were those of an utterly spent and tired muscle, upon which no drug or other therapeutic measure had any lasting influence. His was one of the first cases in which the pale, sickly complexion made an impression upon me.

As the foregoing case illustrates, nothing is at times quite so important in the study of cardiac cases as the determination of the position of the apex-beat. There may be nothing wrong with the heart sounds or the heart rhythm, and yet the apex-beat, by its position, may indicate dilatation or hypertrophy of the heart, or both. When palpating, one must always pass the hand far back into the axillary space. A heart perfectly regular in its rhythm and without a murmur may have its apex there. I well remember the amazement of a post-graduate class when the following circumstance occurred: An elderly woman presented herself in the out-patient department of the Polyclinic Hospital complaining of shortness of breath. One after another of the students examined her and reported irregularity of the heart and nothing else. True, the heart-beat could be felt in about the normal place for it, but great was their astonishment when I showed them a distinct apex-beat in the sixth interspace, midaxillary line. I have always taught that we must consider as the apex the most distant point at which the heart-beat can be felt, and that in some cases of myocarditis though the beat may be forcible in the normal area, the real point of the heart is quite a distance beyond. I am, of course, not considering now displacements of the apex-beat from push or pull, but only those due to enlargement of the heart proper.

The last case I want to discuss with you illustrates so well the beneficial effects of a certain method of treatment that the case has been a source of encouragement to me, and may, I trust, prove so to you.

Mrs. L. was seen in consultation. She was a large, massive woman, who had a huge fibroid tumor of the uterus and chronic myocarditis. She was markedly dropsical and had

a large amount of fluid in her abdomen in addition to the tumor. Aside from enlargement there was little fault to be found with the heart. The soft mitral murmur that could at times be heard was evidently one of relative mitral insufficiency. The whole category of available cardiac remedies had been used to get rid of the dropsy and enable the patient to breathe and lie down. Nearly all of them did good for a time, and then failed. Finally we tapped the abdomen—no easy task on account of the thickness of the abdominal wall and the presence of the fibroid tumor. The tapping helped a little, but the result was not lasting. Gradually the patient became more swollen; her dyspnea grew pitiful; she was forced to sit up in a chair day and night. It was then that we decided to scarify the legs. The result was magical. It is now two years or more, and the woman is alive and in fair health. She is up and about and but little restricted in her activities. We feel sure that the scarification turned the scale. The cuts we made drained for days and days, and removed practically every vestige of dropsy. The drugs that had failed to act before were then able to hold the heart in a state of compensation.

It is entirely unnecessary to use Southey's tubes. All one needs to do is to make with a sharp scalpel several cuts about 1 or 1½ inches long and deep enough to reach the subcutaneous tissue. I usually make them on the inner and outer sides of the calf and behind the malleoli. The serum begins to flow at once. You may scarcely believe me when I say that the oozing fluid may soak dozens of towels in a day. On one occasion, in the Philadelphia General Hospital, I had a tin box with a double bottom made, the upper a coarse sieve on which the patient's unswathed feet rested. In that way I was able to collect most of the extruded fluid, which amounted to 35 ounces in the twenty-four hours. I have never seen any serious infection follow the incisions, probably because the serum is bactericidal. There is no measure, in obstinate cardiac dropsy, that I can recommend more highly.

There is one other therapeutic hint that I want to leave with you—I have found it useful in a number of cases of myocarditis with failing compensation. Gaseous distention is one of the chief

complaints. Much may be done for it by regulation of the diet. Ordinarily the food should consist of milk, buttermilk, well-cooked cereals, chicken broth, custard, junket, orange-juice, occasionally ice cream, with Vichy or other alkaline water as beverage. Some patients, however, do not do well on a diet largely fluid, and have less gas on a diet of chicken, lamb chops, rice, farina, soft-boiled eggs, baked apple, etc. But all too frequently no juggling of the diet has any effect. You may then find the Bulgarian bacillus cultures of great benefit. I prefer the tablets given with a little sugar-water to any other form.

While speaking of remedies I want to call to your attention the little-used drug apocynum cannabinum, which sometimes acts when digitalis fails. I give it in doses of from 5 to 8 drops three or four times a day, and by preference use the strong tincture obtainable at some of the homeopathic pharmacies in Philadelphia. My friend, Dr. Hare, calls this drug the "vegetable trocar." Unfortunately, it does not always make good this reputation.

There exists a group of newer diuretics, chiefly synthetic in nature, that often prove exceedingly useful in cardiac dropsy. One of the best in my opinion is theocin, given in doses of 0.15 to 0.3 gram three times a day. In large doses or too long continued theocin causes nausea.

Failure in the treatment of decompensation is sometimes due to the existence, frequently unsuspected, of hydrothorax, sometimes right sided, sometimes bilateral. The removal of the effusion by tapping will not rarely give to our digitalis therapy a better chance.

CONTRIBUTION OF DR. HENRY K. PANCOAST

UNIVERSITY OF PENNSYLVANIA

THE DIAGNOSIS OF PULMONARY TUBERCULOSIS BY THE ROENTGEN RAY

IN the physical examination of the chest for the diagnosis of pulmonary tuberculosis the essential knowledge to be gained is the determination of the presence of the disease, the extent of lung involvement, the character of the lesion, the chronicity of the process, the prognosis, and the existence of complications. It is our purpose to show how far the roentgen method may simplify the physical examination, confirm its findings, and assist in clearing up doubtful cases. Neither is an exact science, and the accurate determination of all this important data is open to certain sources of error by either method, but it is time for a general understanding of the part roentgenology is ready to play in assisting the clinician. In the diagnosis of the disease the indubitable proof of the presence of a tuberculous etiology is the detection of organisms in the sputum, but, unfortunately, this positive evidence is frequently lacking, and the knowledge of the presence of definite lesions in doubtful cases must, from the clinical standpoint, be based entirely upon the physical signs and symptom complex.

The accurate knowledge of lung conditions that can be gained by changes in percussion note and the effects of lesions upon breath sounds and sound conductivity is truly remarkable, but if, instead of having to mentally construct the lesions producing the changes from normal signs, the gross pathology could be viewed as it exists, how easy and simple the diagnosis would be. The roentgen ray is the one means of bringing patho-

logic lung processes into view, but this visualization is quite different from the direct inspection possible at autopsy, and one must be specially trained to interpret what he sees and to make it conform with definite pathologic conditions. The roentgenologist must, therefore, distinguish the shadows of lesions from those of normal structures, and, in addition, possess a knowledge of pathology to properly identify the former.

If roentgen diagnosis were as accurate in pulmonary conditions as in the detection of urinary calculus or fractures, there could be no question as to its value, and just as much dependence would be placed upon it as in those conditions, but, unfortunately, it is not so generally dependable or exact as yet, especially as it depends so largely upon the personal factors of technic, interpretation, and knowledge of pathology on the part of the roentgenologist. Lesions other than those of tuberculosis sometimes produce appearances indistinguishable from the latter, and the roentgenologist must learn to differentiate these appearances, as does the pathologist the lesions at autopsy. However, roentgen diagnosis is young and physical diagnosis is old, and when the former has reached a small proportion of the years of application of the latter it must follow that improved technic, experience in interpretation, and pathologic knowledge, added to coöperation between the internist and the roentgenologist, will materially lessen the discrepancies now existing. Notable progress has certainly been made during the past few years. The roentgenologist has devoted a large and necessary part of his time to the development of technic and interpretation, but having accomplished much in this direction, he has awakened to the realization of the other factors necessary for diagnostic precision. Many internists who have devoted most of their time to a special study of pulmonary tuberculosis, as, for example, the sanatorium man, have had unusual opportunities for roentgen studies in connection with their clinical work, and their experience has been most profitable to roentgenology. There is no doubt that coöperation between the clinician, pathologist, and the roentgenologist in the future will react most advantageously to all and particularly to the patient.

The foregoing remarks are not intended to belittle the efficiency of roentgen diagnosis, but to remind the clinician that we realize our shortcomings to the smallest detail, and that we are in a position to correct any or all of them. The remarks that follow are intended to convey a correct impression of what may be expected from the roentgen diagnosis from a most conservative point of view.

In the diagnosis of the presence of pulmonary tuberculosis the roentgen examination should be most applicable in two groups of cases. In the first place, it is extremely valuable as confirmatory evidence in a positive clinical diagnosis and in demonstrating the exact location, extent, and character of the lesion. In the second and far more important group, it serves its best purpose as a dependable means of either positive or negative diagnosis in the case with suspicious but doubtful physical signs and negative sputum.

No one doubts the possibility of demonstrating the presence of any pathologic lung changes by the roentgenogram after they have advanced sufficiently far to be readily detected on section of the lung at autopsy, provided the plate details are clear. The question of their proper identification depends upon the accuracy of interpretation. The controversy between the roentgenologist and clinician at the present time centers around the possibility of determining a definite etiologic diagnosis of tuberculosis from certain recognized and supposedly typical roentgenologic appearances, irrespective of the presence or absence of physical signs and organisms. The roentgenologist has but three ways of proving that his contentions are correct: namely, by conformation of the characteristic roentgen features with the physical signs if present, or with the autopsy findings, or by the subsequent progress of the case. His work possesses comparatively little value unless he receives acknowledgment of its correctness, and unless he can substantiate his contentions it is bad taste to make extravagant claims for the superiority of roentgen diagnosis. Unfortunately, autopsy findings are the most valuable and instructive, but the least often realized proof, and especially in cases where confirmation is most important. Coöperation is to

be the solution of the exact determination of the efficiency and accuracy of roentgen diagnosis. Even if this can ever become an exact method, there is no more chance of the roentgenologist assuming the clinician's work than is the case with the surgeon's work in connection with fractures.

The history of roentgenology shows that the roentgen ray has been employed with more or less success in the diagnosis of pulmonary tuberculosis since practically the first year of its discovery. It is interesting to note that Francis H. Williams[1] reported many cases examined by the fluoroscope as early as 1896, at a time when fluoroscopic details of the chest were perhaps far superior to those of plates. In the third edition of his book, published in 1903, he makes the following statement: "Thus far I have been able to detect an abnormal condition of the lungs better by means of the fluorescent screen than by means of the photograph. The screen is a readier and more certain test." This refers to the days of long plate exposures, and was entirely correct. The following fluoroscopic signs are mentioned: "The diseased portion of the lung or lungs is darker than usual, owing to its increased density. The diaphragm is restricted on the affected side or sides, and usually in the lowest part of its excursion. The heart may be drawn toward the affected side, especially during deep inspiration." Although these same observations still hold good, and are recorded as part of our present-day findings, they do not necessarily apply unreservedly to tuberculosis, and have no direct bearing upon an etiologic diagnosis. This he acknowledges in the following sentences: "The signs afforded by the *x*-rays in tuberculosis are not pathognomonic of the disease. We cannot make a final diagnosis of pulmonary tuberculosis by the *x*-rays; but if we exclude the test for bacilli, which cannot be made until cough and expectoration appear, we also see that in the early stage of the disease there is no test that is without question." In some instances even at that time the roentgenoscopic examination revealed conditions not demonstrated clinically, as the following statements show: "In making successive *x*-ray examinations of patients who were suffering from

[1] The Roentgen Rays in Medicine and Surgery, 3d edition, 1903.

tuberculosis at one apex, as indicated both by an *x*-ray and a physical examination, in order to watch the progress of the disease I have observed that, as the process went on, signs were evident in the other apex by an *x*-ray examination before there were physical signs there. Likewise, I have seen by a single *x*-ray examination, when tuberculosis was well advanced, that the disease was more extensive than the physical examination indicated."

A comparatively small intensity of roentgen rays is required for satisfactory roentgenoscopy of the chest, and the tubes and apparatus of the early days were sufficient for fluoroscopic work, but not for making roentgenograms. The extent and accuracy of roentgen diagnosis has kept pace with the improvement in equipment. We might divide the advance in roentgenologic diagnosis of lung diseases into three stages: first, the days of the fluoroscope alone, before sufficient energy could be developed and utilized for rapid plate exposures. The second stage was the beginning of the era of short exposures, when plates with excellent detail were possible but experience in interpretation was immature, and much was taken for tuberculosis that had no connection with the disease. This was, however, the first important step toward accuracy in lung diagnosis. Although a great step in advance had been made when lung exposures of ten to twenty seconds were possible, or while the patient could hold his breath, the real beginning of accurate lung diagnosis was the exposure of one second or less. In 1901 Ziemssen and Rieder[1] published roentgenograms of the lungs made in one second by the aid of intensifying screens. In 1902 Hulst[2] exhibited the first roentgenograms made in this country in one second without screens. The third stage covers the period of the past ten years, during which time the development of tubes and exciting apparatus, refinement in technic, and the making of stereoscopic plates have advanced the work steadily, until the finishing touches are now being acquired through experience in interpretation and a better knowledge of pathology and histology.

[1] Die Roentgenographic in der inneren Medicin, Ziemssen and Rieder, 1901.
[2] Transactions of the American Roentgen Ray Society, 1908, p. 223.

It is needless to say that unless all the modern refinements of the art are brought to bear, the roentgen examination is neither useful nor desirable. Fluroscopy alone is an old and inefficient method, yet even to this day there are men who advocate its use exclusively for the diagnosis of pulmonary tuberculosis. It has its uses, of course, and they are valuable ones, just as inspection and palpation, yet no one who realizes the difficulties and intricacies of accurate lung diagnosis can countenance the employment of this one subsidiary method alone. The great advantage of the roentgenoscope is in the study of moving parts, and this plays an important rôle in eliciting a general knowledge of the case. Again, there are still men who advocate the use of the flat or single plate rather than stereoroentgenograms. To anyone who understands the difference between attempting to interpret numerous superimposed shadows of structures in innumerable planes on the flat plate and viewing and identifying each shadow in its exact position and relations in the stereoscope, the single plate must seem relegated to the stage of progress in which it took origin years ago. Nevertheless, it has its place also, just as has the roentgenoscope, but stereoroentgenograms are absolutely essential in all instances, and sometimes two sets, one made postero-anteriorly and the other anteroposteriorly.

The first important step in the development of accurate interpretation was the recognition of some essential characteristic roentgenologic feature of the tuberculous lesion. Lung structure is so constituted that the air-containing tissue makes it possible to recognize by contrast comparatively slight changes in density and in small areas, and in plates with satisfactorily clear detail these changes can often be recognized almost if not quite as soon as they would be visible to the eye on autopsy section. Cole[1] was the first, in this country at least, to insist upon the recognition of the earliest essential characteristic roentgenographic feature of the tuberculous lesion—the individual tubercle. This term does not imply a roentgenographic recognition of the earliest microscopic stage of tubercle formation, but an actual tuberculous deposit of such size as to be readily seen on cross-

[1] Transactions of the American Roentgen Ray Society, 1908, p. 230.

section of the lung at autopsy. As a single tubercle does not make tuberculosis, he insisted that in order to be indicative of the disease these small shadows must be observed in numbers, either in the parenchyma, roentgenologically speaking, or scattered along or around the larger bronchial tree shadows. Still larger shadows he termed "conglomerate tubercles," and the stage next

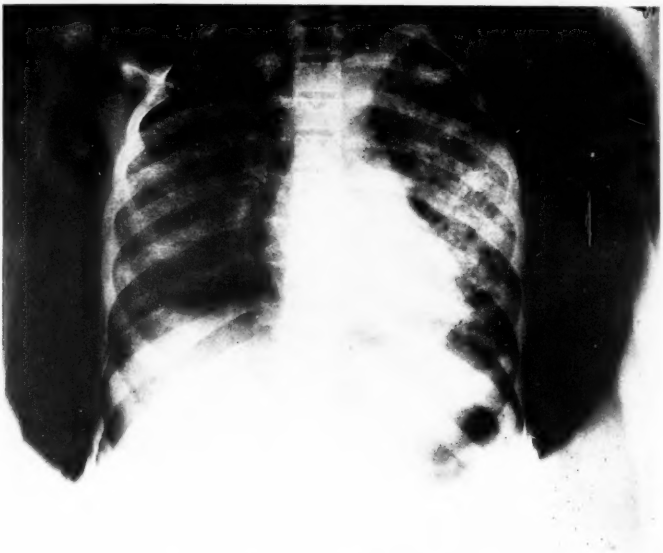

Fig. 17.—Pulmonary tuberculosis, bronchopneumonic type. Patient a female aged fourteen years. Stereoroentgenograms showed diffuse infiltration with individual and conglomerate tubercles and small consolidations throughout both lungs. This might be a case of miliary tuberculosis from the roentgen standpoint, but it was not clinically. In small reductions, individual tubercles are too small to be readily seen. The mottled appearance here shown is due to the larger lesions —the conglomerate tubercles and small consolidations.

in size shadows indicative of small consolidations (Fig. 17). Needless to say, these appearances must be found in the usual distribution of pulmonary tuberculosis. In describing diffuse infiltrations throughout the lungs the term "miliary tuberculosis" is frequently misapplied, and should be reserved to designate the pulmonic manifestation of the general systemic infection.

From the roentgenologic standpoint this classification proposed by Cole has stood the test of time, and is no doubt a permanent fixture, notwithstanding the criticism it has developed from time to time. It is purely a roentgenologic classification based upon pathologic processes. Multiple individual tubercles are generally accepted as comprising the earliest roentgenologic evidence of pulmonary tuberculosis. Dunham, however, has described an appearance which he interprets as indicative of a still earlier stage of the disease. It is practically a hazy fan-shaped area in the parenchyma, at the terminations of the branching lines of a bronchial trunk shadow, usually the vertebral or the first or second interspace trunks. It is supposed to represent the effect of congestion and exudation resulting from the early tuberculous process, before the stage of formation of distinct individual tubercles. There is ample proof that such appearances have later developed into undoubted evidences of tuberculosis, but they are exceedingly difficult to recognize, are not so typical as Cole's characteristic appearances, and, in fact, there is much question as to whether they are typical of the disease. They may be stimulated by other conditions, such as an early pneumonia or the early stage of an infarct.

Based upon the anatomic distribution of the disease, roentgenologists now recognize three manifestations of the disease, at least in the earlier stages, namely, the hilus lesion, peribronchial infiltration along the larger subdivisions of the bronchial tree, and infiltration in the parenchyma further out around the bronchi, and their terminations. Of course, most infiltration is more or less peribronchial and in the parenchyma, and this classification may seem ambiguous, but is not incorrect when viewed from the roentgenologic standpoint, and serves a very important purpose of distinction. For example, the evidence of peribronchial infiltration is not so typical as that of infiltration in the parenchyma, and, according to Heise and others, peribronchial infiltration from the roentgen standpoint denotes a more chronic process and one more likely to heal than the infiltration in the parenchyma.

Hilus Lesions.—The roentgenographic appearance of a lesion

primary in the hilus structure presents nothing typical of the disease. There may be an increase in the dimensions or density, or both, of the usual hilus shadow, more or less homogeneous throughout, or irregular and suggestive of glandular elements (Fig. 18), but this same appearance may arise from other con-

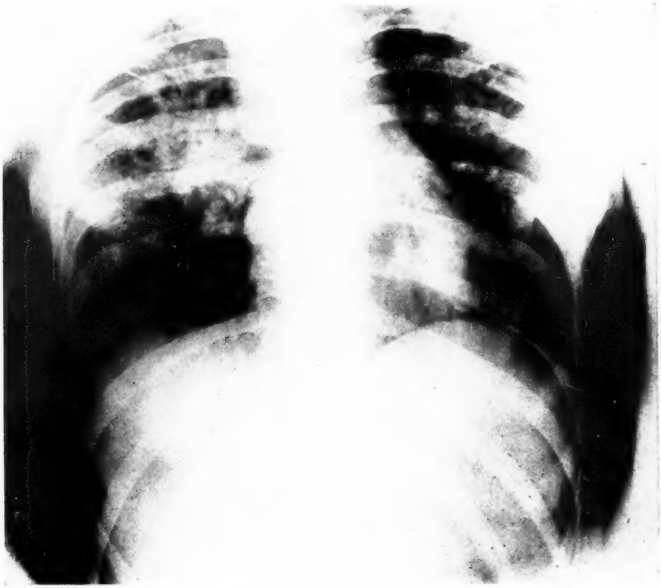

Fig. 18.—Hilus tuberculosis, right side, with infiltration spreading out into lung. Also infiltration of left apex. Patient a female aged sixteen years. Tuberculous glands excised from neck. Stereoroentgenograms showed an appearance quite like a mediastinal neoplasm, but no doubt due to enlarged glands and a hilus lesion. Extending outward from this area was an infiltration, with individual and conglomerate tubercles. This is not a typical distribution of tuberculosis, but the patient was known to have the disease and the roentgenograms showed the location, extent, and character of the lesions.

ditions. It is always found in the early stage of pneumoconiosis, may be observed in apparently healthy individuals, and may be simulated by new growths. Even though a positive etiologic diagnosis cannot be based upon such an appearance, the roentgenogram has its distinct value. Physical signs may be absent, in-

definite, or lacking in any features indicative of the presence of the disease or its location. The etiologic diagnosis must, if possible, be primarily a clinical one, in which case the roentgen examination serves to indicate the presence of a hilus lesion and to show its extent. The case in which such a lesion is usually

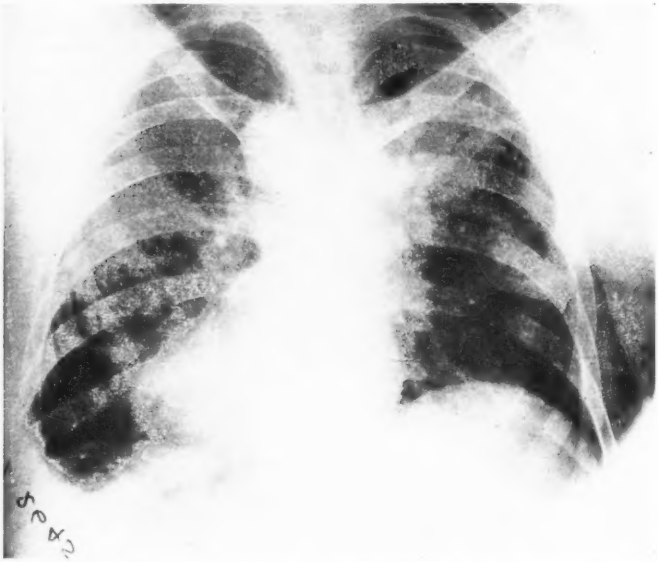

Fig. 19.—Diffuse pneumoconiosis, with fibrosis just beginning in the right apex. Patient a male aged forty-seven years. He worked around mines for thirty-eight years, but always outside. (Compare with Fig. 22.) Roentgenoscopic examination showed no interference with diaphragmatic movements. Stereoroentgenograms showed diffuse pneumoconiosis with fair-sized, prominent, discrete spots, distributed on both sides from bases to apices, and more marked on the right side, as is always the case.

demonstrated is one presenting the general symptom-complex of a tuberculous patient, with slight evening temperature, slightly accelerated pulse-rate, poor circulation, under weight and "below par," and with a cough, with or without organisms in the sputum. Physical signs may be indefinite or absent. If the appearance in the roentgenogram suggests a hilus lesion and no

other manifestations, it may be regarded as lending confirmatory evidence to the clinical diagnosis, as well as indicating the seat and extent of the lesion. There may, of course, be instances of unquestionable hilus involvement in addition to other manifestations (Fig. 19). In the hilus manifestation the therapeutic procedure must be governed by the clinical aspect of the case.

Peribronchial Infiltration.—This term is employed to designate an infiltration which appears to be limited to the structures along the larger subdivisions of the bronchial tree, and the roentgenologic features are a thickening of the bronchial trunk shadows extending upward or outward from the hilus in the usual early distribution of the disease to the extreme apex or the anterior portions of the first or second interspaces, or, in plates presenting unusually fine detail, there may be observed some fine mottling representing visible individual tubercles along the thickened trunks. That such lesions can be demonstrated by the roentgenogram, and that such appearances may be indicative of tuberculous lesions, is beyond question, but the appearance is by no means typical or always indicative of a tuberculous process. Single or multiple thickened bronchial tree shadows in the regions just described are quite common in apparently healthy individuals who do not have tuberculosis, especially in those following dusty occupations. The thickened trunk shadows may also follow other infections, like whooping-cough or influenza.

Again, in this manifestation the etiologic diagnosis must, as a rule, be primarily a clinical one, or the disease must at least be suspected from the general symptom complex. There may or may not be bacilli in the sputum, and the latter may be occasionally blood tinged. If the roentgenogram presents the appearance described, and there are no other manifestations, it can usually be regarded as confirmatory evidence, and as indicating the location, extent, and character of the lesion when there are organisms in the sputum. In the absence of organisms, however, it should not be given so much recognition unless there are at least some indefinite physical signs over the particular area. Even though the roentgenogram does not present indubitable evidence of an etiologic diagnosis in such cases, it has, neverthe-

less, a distinct diagnostic value. It may also show that the lesion is of comparatively mild severity, and may often be of service in aiding to outline the policy of treatment.

Lesions in the Parenchyma.—This term applies to the more frequent manifestations of early tuberculosis, and implies the presence of individual or conglomerate tubercles in the regions around the bronchioles and their terminations, where the shadows of the latter have ceased or have become fine lines. This is the only one of the three roentgenologic manifestations of the disease that presents a typical roentgenographic appearance. That the appearance is indicative of a tuberculous lesion in most instances there can be no doubt, but that it indicates an etiologic diagnosis of the disease in every instance cannot be accepted, even though it is found in the usual distribution of tuberculous lesions. The small shadows indicative of individual tubercles may be simulated by pneumoconiosis arising from very numerous occupations and also by certain mycotic infections. Usually, however, the distribution of the shadows will serve to distinguish tuberculous lesions from those arising from other causes, although exceptions must be recognized. The appearance of early diffuse infiltration is often hardly distinguishable from that seen in marked pneumoconiosis, before the stage of fibrosis, when the distribution is wide-spread, but the clinical aspect of the case will usually serve to differentiate the conditions, and in later stages of diffuse infiltration more advanced lesions, such as consolidations and cavities, are usually to be found in addition to the tubercles (Fig. 20).

In view of these facts, it does not seem to be a justifiable procedure to base an unqualified etiologic diagnosis in this type of case upon the roentgenogram alone, irrespective of clinical evidence, although it may be safe in the large majority of instances. This statement must be modified or viewed in a different light to suit certain circumstances based upon the qualifications of clinical and roentgenologic examiners. It is an unfortunate fact that all medical men do not possess equal diagnostic abilities. We must recognize the mediocre roentgenologist and clinician as well as those who are expert in their lines. The former com-

bination is an unfortunate one when drawn together, but the latter obtains the most accurate results when working in coöperation. The mediocre roentgenologist is of no particular use to the able internist, but the experienced roentgenologist is likely to aid materially in checking up the inexperienced physician. There can be no doubt of the value of efficient roentgenologic work

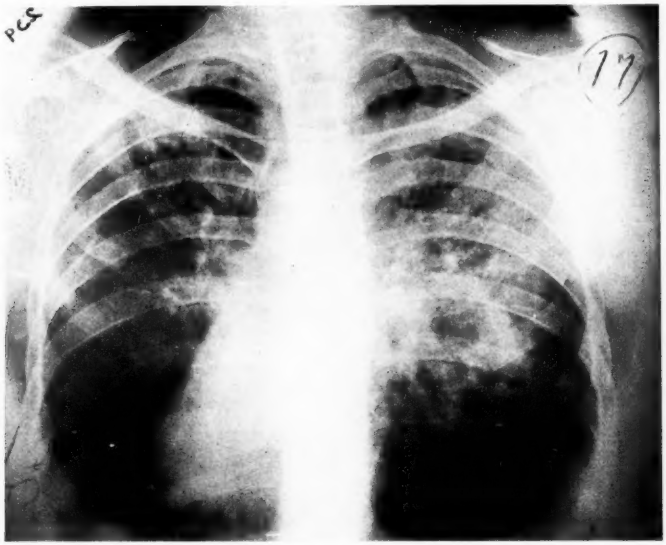

Fig. 20.—Fibrosis resulting from pulmonary tuberculosis. Patient a male aged forty-four years, and clinically presenting a long history of chronic tuberculosis, but now quiescent. The left lung was the seat of the more recent process. Stereoroentgenograms showed fibrosis both sides, mainly in bands, but also in areas representing tubercles and smaller consolidations. Some of the latter will be seen to be very dense and possibly calcified. There were some bronchiectatic cavities. The distribution is that of tuberculosis.

in the diagnosis of pulmonary tuberculosis. A roentgen examination is, of course, not essential in every case, although it may be desirable and instructive, especially in institutional work. Its greatest value is in the doubtful case, and in the more certain ones where a knowledge of the extent and character of the lesions is desired.

Chronicity.—The claim is frequently made that the roentgenogram will determine activity in a tuberculous lesion. This may be done in some instances, but the differentiation of the stages of activity, unless widely separated, is usually more theoretic than practical. The determination of activity depends upon the differentiation of slight shadow densities. It is very

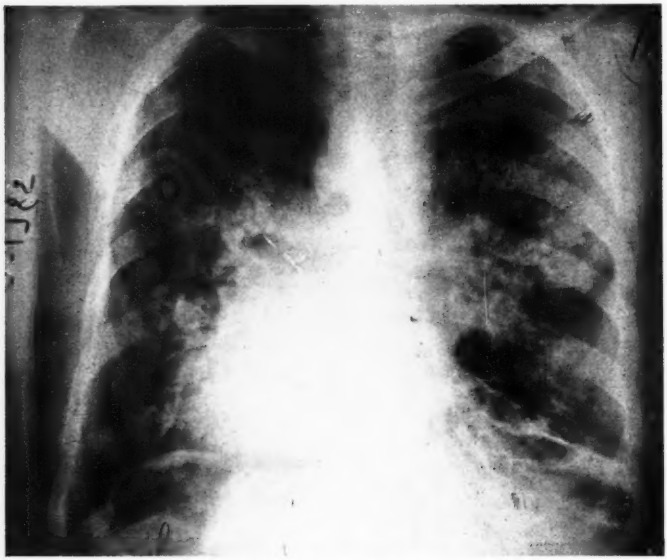

Fig. 21.—Fibrosis resulting from infection following inhalation of foreign body. Patient, a male aged twenty-nine years, inhaled a vegetable burr when a child. Cough and profuse expectoration. Roentgenoscopic examination showed numerous bronchiectatic cavities at the right base which could be seen opening on inspiration and collapsing on expiration. Stereoroentgenograms showed, in addition, an extreme fibrosis of both lungs. No tubercle bacilli in the sputum.

easy to determine the difference in density between an active lesion, with individual or conglomerate tubercles of comparatively recent origin, and similar old chronic lesions that have undergone complete fibrous change or calcification, because of the great difference in densities of the shadows. But it is not so easy to differentiate between the new active lesion and the one that has undergone slight fibrous change. It should be borne in mind

that active and quiescent lesions frequently coexist. The *chronicity* of a lesion is far more readily determined and with greater accuracy, depending upon the amount of fibrosis. Activity must usually, though not always, of course, be determined clinically.

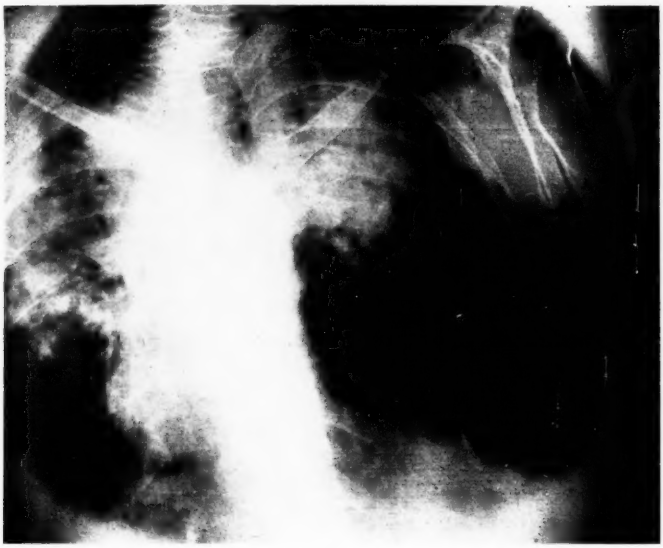

Fig. 22.—Extreme fibrosis resulting from pneumoconiosis. Patient, a male aged fifty-one years, had worked inside a coal mine thirty years. (Compare with Fig. 19.) Roentgenoscopic examination showed fixation of both diaphragms. Stereoroentgenograms showed bronchiectasis and extreme fibrosis throughout both lungs. The appearance is most marked in the apical regions, simulating tuberculosis. Large spots representing pneumoconiosis still visible. Repeated sputum examinations negative.

In addition to the characteristic lesions and the manifestations already referred to, there are certain end-results that can be recognized in the roentgenogram, namely, fibrosis, consolidation, calcification, cavity formation, and bronchiectasis.

Fibrosis.—Until recently there has been a prevailing idea among roentgenologists that fibrosis is a condition peculiar to pulmonary tuberculosis, hence its appearance has been a fre-

quent source of error in interpretation. One has only to study cases presenting fibrosis arising from other sources, such as dust inhalation, in which it follows as the terminal stage of pneumoconiosis, to realize the difficulty in accurately determining the tuberculous etiology in a case of fibrosis in which

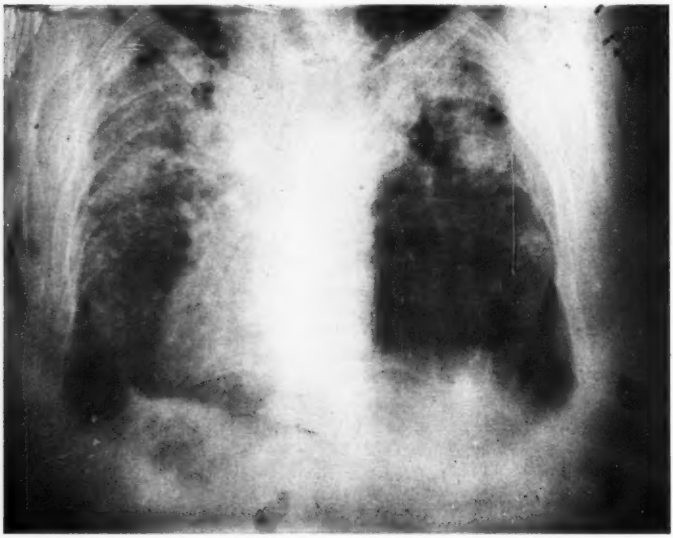

Fig. 23.—Extreme fibrosis in a case of so-called "potters' asthma." Patient, a male aged fifty-five years, had worked in a pottery for forty-five years. Roentgenoscopic examination showed absolute fixation of the diaphragms, hence the very marked dyspnea. Stereoroentgenograms showed extreme fibrosis throughout both lungs, most marked in the apical regions. He had previously been sent to a tuberculosis sanatorium, but was discharged because of negative sputum. Eight repeated examinations since the roentgenograms were made were also negative.

the previous history is lacking. Indeed, in order to intrepret the appearance of fibrosis as tubercular in origin, one must prove an antecedent tuberculous history or be able to demonstrate conclusively the typical roentgen appearance of tuberculous lesions along with the fibrosis (Figs. 20–23). The distribution alone is not the deciding factor in all instances,

as the cases of pneumoconiosis in which fibrosis is just beginning or has advanced considerably show the fibrous changes most marked in the apical regions where tuberculous lesions predominate. In many cases of industrial fibrosis it is impossible to distinguish the appearance from tuberculosis or to determine whether or not there is a coexistent tuberculous process present. The general even distribution of discrete spots in pneumoconiosis, where fibrous changes are comparatively early, is a safeguard, and one should suspect this origin of the fibrosis and inquire into the occupational history as well as into a tuberculous history.

In the detection and location of cavities resulting from the breaking down of consolidations the roentgen examination serves a most useful purpose. Bronchiectatic cavities are frequently more difficult to find, but they can usually be diagnosed. In the differentiation between the two forms of cavities, one must be guided by the location, surrounding appearance, and often by the history of the case.

Complications.—The complications of pulmonary tuberculosis that are subject to satisfactory roentgen study are mainly in the pleural cavity, comprising empyema and pneumothorax. It is needless to dwell upon the importance of the roentgen examination in these conditions.

Conclusions.—1. The characteristic roentgen feature of early pulmonary tuberculosis is the individual or the conglomerate tubercle when found in numbers. The appearance is usually typical of the disease, but not always.

2. From the roentgenologic standpoint early pulmonary tuberculosis may manifest itself in three ways, depending upon the anatomic distribution—the hilus lesion, peribronchial infiltration along the larger trunks, or infiltration in the parenchyma further remote from the larger subdivisions of the bronchial tree.

3. Fibrosis may result from tuberculosis, but when seen does not necessarily imply a tuberculous process.

4. A roentgenologic study of every case is not essential. Its greatest value is to determine the exact nature and extent

of the lesion when the diagnosis is certain and to assist in the diagnosis of doubtful cases.

5. The policy of treatment is largely to be determined clinically when the diagnosis is assured, although the frequent aid of the roentgen examination is not to be denied.

6. The best interests of the patients are served by coöperation between a competent clinician and roentgenologist.

CLINIC OF DR. A. A. STEVENS

PHILADELPHIA GENERAL HOSPITAL

ANGINA PECTORIS AND ALLIED CONDITIONS

Report of a Case with Discussion of the Symptoms. Angina Abdominis. Varieties of Angina Pectoris. Etiologic Factors. Prognosis and Therapy.

THE case that I present today is interesting chiefly because it illustrates two or three of the more serious concomitants of cardiovascular disease.

The patient is fifty-two years of age, an American by birth, and a printer by occupation. The family history is good. His mother is still living at the age of eighty years; his father died at about the age of seventy of pneumonia. He married twenty years ago, but his wife died of nephritis within a year after her marriage. He has been a very heavy smoker from his nineteenth year until a few months ago and is a moderate drinker; he has never worked hard with his muscles. At the age of twenty-five he had syphilis, for which he was inadequately treated. With this exception he has always been well and strong. His present symptoms began about three years ago, with slight shortness of breath and a sense of oppression in the chest on walking fast. After resting for a minute or two these sensations would rapidly disappear. Any unusual effort, however, would cause their return, although, as he states, if he "took it slowly" he could subsequently exert himself to a considerable extent with scarcely any discomfort. There was at first no actual pain, but one day about two years ago, after carrying a heavy box, he felt an indescribable distress in the region of the heart, perspired freely and vomited, and for a few minutes was unable

to move. This experience marked the beginning of a series of attacks, some small, as he terms them, and others of great intensity. For a long time the pain appeared only upon undue muscular exertion, but of late on several occasions there have been paroxysms during repose. The pain, in the more severe attacks, radiates from the region of the heart up the neck to the head and also down the left arm. It is frequently accompanied by nausea or vomiting and copious sweating, but rarely, if ever, by any sense of imminent death. The seizures last five to ten minutes and cease abruptly, the end being marked, as a rule, by noisy eructations of gas. In some of the milder attacks the patient finds relief in slowly walking about, but when the pain is severe he is unable to stir until it subsides. After the paroxysm he is much depressed, and his left arm feels weak and numb for an hour or more.

During the last year the patient has had at least three attacks in which the pain was confined to the abdomen, especially to the region of the umbilicus, and was accompanied by marked tympanites and extreme sensitiveness of the abdominal wall. The pain, he states, was intense, lasted two or three hours, and always culminated in vomiting. Except as a result of muscular effort there has not been until recently any noticeable shortness of breath, but within the last month the patient on several occasions has been seized at night with severe dyspnea. These asthmatic attacks have usually come on independently of pain, but about a week ago a feeling of great uneasiness in the region of the heart first appeared, and this was followed by dyspnea lasting all through the night. An examination of the chest by the intern during the seizure revealed numerous musical râles with prolonged wheezing expiration.

At present the patient is fairly comfortable. You will note that he is well nourished, but somewhat pale. The peripheral arteries are thickened and slightly tortuous. The pulse is regular, full, hard, and 90 a minute. The maximal pressure varies between 165 and 180 mm. Hg. The apex-beat is visible just within the midclavicular line. There are no areas of abnormal pulsation. The area of relative cardiac dulness is not increased. The note

over and around the manubrium is clear. The aortic second sound is a little accentuated, otherwise the sounds are normal. Except for a moderate grade of emphysema the lungs appear to be normal. Examination of the abdomen is negative. The urine has a specific gravity of 1016, shows a mere trace of albumin, and contains a few hyaline casts. The phenolsulphonephthalein excretion in two hours is 68 per cent. The blood yields a frankly positive Wassermann reaction.

Symptoms.—The diagnosis of the patient's chief complaint is, of course, obvious. The character and distribution of the pain, the evidence of syphilis, the condition of the blood-vessels, and the associated dyspnea, all proclaim the case to be one of angina pectoris. The pain has the usual irradiation—that is, into the neck and down the inner surface of the left arm—and this feature is to be regarded as an example of "referred sensation" in the sense of Head and of Mackenzie, irritation arising in the heart or aortic arch, which are insensitive, being conducted to the corresponding visceral segments of the spinal cord, that is, to the upper thoracic segments, whence impulses arise which are projected along the upper thoracic spinal nerves to the periphery, where they are recognized as pains. In some cases the pain radiates down both arms, and occasionally it is felt in the right arm only. Frequently, the most intense pain is in the region of the elbow. The extension of the pain into both arms has been explained on the theory that the peripheral irritation is sufficiently intense to pass over from one side of the spinal cord to the other, and the radiation of the pain into the right arm alone, on the theory that the nerve-endings in the wall of the right ventricle only have become irritated. As noted by Heberden, the pain in the arm may precede the angina for years. The pain is occasionally experienced chiefly in the epigastrium, and when this is the case it is likely to be misinterpreted, especially at first, and to be ascribed to some disorder of the stomach. After an attack the skin over the parts in which the pain has been felt is often hypersensitive. It has been shown by Eichhorst and by Gibson that wasting of the muscles and changes in the texture of the skin may also be found at times in the

painful regions. The pain varies much, both in degree and kind. There may be merely a feeling of oppression about the heart or aching beneath the sternum, or there may be an overwhelming sense of constriction in the chest. Many patients feel as if the heart or the whole chest were being squeezed in a vise. In *angina major* the pain is usually accompanied by a feeling of alarm or dread, and in some cases by a terrible sensation of imminent death. In *angina minor*, or what has been termed the *petit mal* of the disease, the pain is, as a rule, comparatively mild, does not travel far from its starting-point, and is not often accompanied by any pronounced feeling of imminent dissolution. Attacks of angina major and of angina minor not rarely alternate with one another in the same subject, and in many cases the mild attacks appear first and later are superseded by the severe ones. The mental anguish is a distinct feature of the process and does not run parallel with the pain. Occasionally attacks are observed in which the pain is subsidiary and the sense of dying is the conspicuous element. To seizures of this type Gairdner gave the name of *angine sine dolore*.

Except in paroxysms that prove fatal consciousness is not often disturbed. In exceptional instances, however, the heart pang is followed by syncope. Occasionally, too, the same lesion that is responsible for angina pectoris also results in heart-block, and then syncopal, vertiginous, or even epileptiform seizures may accompany the heart pain, but rather as a part of the Adams-Stokes syndrome than of the angina itself.

Vasomotor disturbances are rarely absent in angina major. The skin is usually pallid, cold, and covered with sweat, but sometimes the face is suffused, or even congested, and the surface veins may be unduly prominent. It is generally believed that even when the arterial pressure is normal between the attacks the pressure rises the moment the pain appears. This is true, however, only of a certain proportion of cases. Very often the blood-pressure shows no material change one way or the other during the paroxysm, and not rarely it is actually

lowered. In many cases as the symptoms subside large quantities of urine are passed.

Not only may the pain be referred to the epigastrium, but gastric symptoms may be so conspicuous as to lead to errors in diagnosis. Frequently the attack is accompanied by nausea, flatulency, and hiccup, and occasionally, as in the present instance, vomiting occurs. At the end of a paroxysm there are often noisy eructations of gas, and to these the patient is likely to attribute his relief.

In the case that I present to your notice physical examination of the heart itself reveals nothing abnormal, with the exception of a slightly accentuated second aortic sound. The area of cardiac dulness is not increased; there are no adventitious sounds, and the rhythm of the contractions is regular. Nevertheless, the condition of the patient's arteries, his breathlessness on exertion, his paroxysms of pain and nocturnal asthmatic seizures make the presence of myocardial disease certain, and that of sclerosis of the coronary arteries highly probable.

This case affords an excellent demonstration of the fact, clearly taught by clinical experience, that subjective disturbances are, as a rule, the most trustworthy indications of the heart's efficiency. Unfortunately, extensive lesions of the ventricular wall may be present without giving rise to either symptoms or signs, because, as it has been expressed, a large part of the myocardium is *silent*, this term being used in precisely the same sense as when applied to certain areas of the brain. Signs of organic disease of the heart or aorta are, of course, not always lacking. In some instances you will find a soft systolic murmur at the apex. This may be merely incidental, and its cause in no way related to the angina, or it may be an indication of myocardial weakness. Much more frequently a systolic or diastolic murmur is heard at the base of the heart, aortic valvular disease, especially insufficiency, being found more commonly in association with angina pectoris than any other lesion except sclerosis of the coronary arteries, and in a large number of cases both of these conditions are present. In cases of syphilitic aortitis, a lesion with which angina is often

associated, a diastolic murmur may make its appearance for the first time many months after the onset of the pain. In other cases there are definite signs of an aneurysm involving the arch of the aorta, especially the ascending portion. In some instances the presence of degenerative changes in the muscular tissue of the heart is made evident only by the occurrence of an abnormal rhythm. Finally, in a few cases there are indications of pericarditis. The pericarditis may be antecedent to the paroxysms of pain. For instance, in the cases of true angina occasionally observed in children adherent pericardium is not an uncommon association. The occurrence of a pericardial friction has been noted in several instances of angina in which the attack was precipitated by sudden occlusion of a coronary artery and the production of an area of myocardial softening. Again, the pericarditis may be incidental and unrelated to the angina. Thus, in cases of cardiorenal disease, which are sometimes associated with angina, the patient after reaching the uremic stage not infrequently succumbs to a terminal infection involving the pleura or pericardium.

Etiologic Factors.—In the case before us the blood-pressure is comparatively high, the peripheral arteries are stiff and tortuous, and the second aortic sound is somewhat accentuated. These are indications, of course, of arterial disease, and this always makes possible the occurrence of angina pectoris, especially if it involves the coronary arteries. There is no very close relation, however, between high blood-pressure itself and anginal attacks. Janeway reports that of 100 cases of hyperpiesis, in which accurate information as to the important later symptoms and the exact cause of death was obtained, anginoid pain on exertion was a symptom in 15, and in only 2 was death due to the angina. Gradual cardiac insufficiency, uremia, and cerebral apoplexy were the most frequent causes of death.

The pathologic lesion responsible for angina pectoris is usually sclerosis of the coronary arteries with myocardial degeneration or disease at the root of the aorta, just at the openings into the coronary arteries. Huchard found coronary sclerosis in 128 of 145 autopsies recorded in the literature, and

in most of the others either valvular disease or adherent pericardium. The changes in the vessels may be those naturally occurring with advancing years or those brought about by syphilis, gout, Bright's disease, etc. Syphilis is a very potent factor, and in young or middle-aged men the provocative lesion is frequently an aortitis characteristic of this infection. Some of the worst attacks of angina pectoris are due to the more or less sudden occlusion of a large branch of a coronary artery by a thrombus.

While undoubtedly a close relation exists between anginal seizures and cardiovascular disease, it must be recognized that many patients with coronary sclerosis and seriously damaged hearts suffer no pain, and, on the other hand, that severe attacks of cardiac pain occasionally occur in the absence of any demonstrable lesion in the coronaries, aorta, or myocardium. In this and other hospitals for the indigent true angina pectoris, at least the major form of the disease, is comparatively rare. The case before us is the first that I have seen in this hospital in more than a year, although in the same period there have been hundreds of patients with cardiovascular disease in its most extreme forms. To account for the absence of pain in these cases it is necessary to recognize the presence in angina pectoris of another factor besides the organic lesion. What this elusive factor is we do not definitely know. It probably has to do, however, with the sensitiveness to stimulation of the central nervous system, which is much more pronounced in some individuals than in others. With an extremely sensitive nervous system there may be attacks of severe pain, even if the heart is only slightly damaged. If this hypothesis is correct, it affords an explanation of the marked contrast between the incidence of angina in hospital and in consulting practice. The frequency with which physicians, lawyers, actors, and others who are subjected to severe mental or emotional strain are attacked has been commented upon by several writers. In certain individuals the hypersensitiveness of the nervous system appears to be so pronounced that pain is produced with great facility. Indeed, it is possible that in such persons angina may occur in the ab-

sence of any appreciable organic change in the heart or aorta. This type of the disease has often been referred to as pseudo-angina, but the term is not a good one, and has been largely superseded by that of *functional angina pectoris*, the latter form, which rarely, if ever, proves fatal, is, as a rule, readily differentiated from the organic variety, although in some cases the diagnosis is difficult or even impossible.

Functional angina is observed, as a rule, in persons of a neurotic temperament. It occurs usually in younger persons than the organic form, and is much more frequent in women than in men. The onset is often without an apparent exciting cause; the attacks usually last longer and end less abruptly, and the pain, which is rarely so severe as that of organic angina, is often accompanied by marked vasomotor disturbances, but seldom, if ever, by the sense of impending death.

Tobacco.—The question of the effect of tobacco on the heart has been much discussed, and yet accurate information on the subject is still meager. There is, however, incontrovertible evidence that nicotine can change the caliber of the blood-vessels, in some cases causing constriction and in others dilatation, and that it is also capable of inducing a great variety of cardiac irregularities similar to those resulting from stimulation of the cardiac nerves, either singly or together, or from stimulation of the one and paralysis of the other. These disturbances seem to be merely functional, and soon subside on the discontinuance of the drug. The evidence that excessive smoking can produce organic change in the vessels and heart is not so convincing, although the results of certain recent investigations point strongly in this direction. Turning to clinical testimony, we find that many observers of large experience, among whom may be mentioned Huchard, Erb, and Klemperer, declare that without doubt tobacco can produce arteriosclerosis, myocardial degeneration, and other circulatory disorders. Whether this is true or not, it is universally admitted that excessive smoking is quite capable of provoking anginal attacks in individuals who already have organic disease, and that the pains often disappear rapidly after the complete withdrawal of the drug. It is

not unlikely also that tobacco may sometimes cause such intense irritability of the nerve-centers that slight perturbations reaching them from the heart may result in pain, even in the absence of any organic changes. Experience shows that the injurious effects of excessive smoking are materially increased by the simultaneous abuse of alcohol.

Certain poisons other than tobacco, by irritating the heart, may also act as provocatives in susceptible subjects. In a patient with chronic cholecystitis whom I recently attended every acute exacerbation of the gall-bladder disease was attended by attacks of severe cardiac pain, breathlessness, and arhythmia. Mackenzie cites the case of a woman in whom anginal attacks of the most agonizing description completely disappeared upon the evacuation of a pelvic abscess.

Cause of Pain.—As to the actual cause of the pain in angina pectoris we are still in doubt. Lancereaux and Peter believed it to be due to a neuritis of the cardiac plexus of nerves. Heberden and Latham ascribed it to cramp of the heart muscle. Traube, Lauder Brunton, and many others have held that it is the result of overdistention of the ventricles, and, therefore, of the same nature as that produced by overstretching of other hollow organs, such as the stomach, bowel, and bladder. Allbutt for many years has maintained against much adverse criticism that anginoid attacks are the direct outcome of disease of the aorta, more especially of that part of it just above the sigmoid valves, and that the immediate cause of the pain is undue tension of the fibrous outer coat of the vessel. Perhaps the most plausible theory is that of intermittent claudication, originally suggested by Allan Burns, of Glasgow, in 1809, later advocated by Potain, and in recent times ably defended by Osler. According to this theory, the attack of pain is due to transient ischemia of the heart muscle, and is likely to occur whenever there is a marked disproportion between the amount of blood needed by the myocardium and that which the coronary arteries are able to deliver to it. In intermittent claudication, or intermittent limping, the arterial blood-supply to the lower extremities is interfered with by an obliterative arteritis. So long as the affected

parts are quiet there may be no symptoms, but any sudden exertion which makes necessary a copious supply of blood to the muscles results in an abrupt loss of power, cramp, and sometimes acute pain. These symptoms rapidly disappear under rest, but are likely to recur whenever the muscles are actively used. The phenomenon is sometimes the precursor of gangrene. Another condition that seems to belong to the same category as angina pectoris and intermittent claudication is the transient hemiplegia or aphasia that is frequently observed in elderly persons who have sclerosis of the cerebral arteries.

Exciting Cause of Attacks.—In the majority of cases of organic angina the attacks occur only in response to some exciting cause. The most important factor is muscular effort. Walking up hill or against the wind is especially liable to bring on a paroxysm. In extreme cases such slight exertion as raising the arm above the head may cause pain. Mental emotion is also potent; even fear of attack may precipitate one. In some patients digestive disturbance is the most common exciting cause, although in this connection it must be pointed out that gastric symptoms, such as belching and nausea, are often the result of an attack rather than its cause. Less frequently patients with angina ascribe their attacks to exposure to cold. The occurrence of angina without any apparent exciting cause usually means one of two things: namely, that the changes in the heart or aorta have reached an advanced stage, or, on the other hand, that the paths of pain are exceedingly irritable, which seems to be the case in the functional or non-fatal form of the disease. In some instances, however, the attacks arise, as it were, spontaneously because of the presence of some toxic condition, such as may result from infection or the excessive use of tobacco. Under these circumstances the removal of the toxic element may cause the pain to disappear, or to occur only in response to muscular effort or mental emotion.

Angina Abdominis.—In the case before us you will recall that the pain on several occasions was entirely confined to the abdominal region and was accompanied by marked tympanites and extreme sensitiveness of the abdominal wall. It may be

interesting for us to consider for a moment this somewhat unusual localization of pain in a case of the kind under consideration. There are a number of conditions arising from cardiovascular disease which may cause severe abdominal pain. As I have said, the pain of ordinary angina pectoris is sometimes referred in part to the lower end of the breast bone, and occasionally the maximum intensity of the distress is in the epigastrium. In the violent and usually fatal seizures which are brought on by complete stoppage of the coronary arteries the pain is often referred definitely to the upper abdomen. In cases of myocardial failure with symptoms of general venous stasis, such as dyspnea and edema, persistent epigastric pain of a dull, aching character, intensified by pressure and often by the ingestion of food, is usually associated with an enlarged, congested liver, which in the majority of cases can readily be made out by palpation. Another cause of acute abdominal pain in the course of advanced cardiovascular disease is embolism or thrombosis of the mesenteric vessels. This complication usually results in hemorrhagic infarction of the intestine, acute peritonitis, and death within a few days. The pain, which is often intense, is generally accompanied by abdominal distention, bloody diarrhea, and symptoms of shock. Embolism of the spleen may produce a similar clinical picture, although in most cases the pain is referred to the left side. Occasionally sclerosis of the arteries in the mesentery or bowel, in the absence of embolism or thrombosis, is responsible for recurrent crises of pain in the abdomen similar in many respects to those occurring in the chest in ordinary angina pectoris. This condition has been given a variety of names, although it is usually known by that of *angina abdominis*, which was first used by Bacelli. The attacks occur, as a rule, independently of the ingestion of food, and are more liable to develop when the patient reclines than are those of angina pectoris. Besides the pain there are usually several other features, including paroxysmal hypertension of the pulse, transient paralysis of the segment of bowel involved, with constipation and meteorism. Vomiting may also occur, and in some of the cases the abdomen is so sensitive during the seizure

that the weight of the bedclothing is unbearable. Differentiation is difficult, but it is possible when manifestations of arteriosclerosis elsewhere give the clue. The close resemblance at times of this syndrome and other painful abdominal crises, the result of arteriosclerosis, to various surgical conditions involving the abdominal organs, such as perforation of a peptic ulcer, acute intestinal obstruction, and acute hemorrhagic pancreatitis, is worthy of emphasis. In the patient before us the recurrent attacks of acute abdominal pain may well be those of angina abdominis, as they are not merely epigastric, but center definitely around the umbilicus, and are associated with signs of general arterial disease and with other paroxysms that are clearly those of angina pectoris. Of course, in the presence of syphilis, of which there is positive evidence in this case, one must also think of the possibility of tabetic crises, particularly as a close relationship is known to exist between syphilis, on the one hand, and locomotor ataxia and arterial disease, especially lesions of the aorta, on the other. Thus, in analyzing the autopsy records of 34 cases of locomotor ataxia, Burr found that atheroma of the aorta was specifically mentioned nine times, and that aneurysm of the aorta was present in 3 cases. Opposed to the diagnosis of tabes in this case, however, are the lively knee-jerks and the absence of pupillary changes, of vesical disturbances, and of Romberg's sign.

The **prognosis** of organic angina pectoris is very uncertain. Death may occur with the first attack or with the second or third, or in one of a series of rapidly occurring attacks. On the other hand, a patient may have recurring paroxysms over a period of twenty years or longer, and not very rarely the pains disappear entirely, the patient appearing apparently well for years. In some cases, as Musser pointed out fully twenty years ago, the pains cease upon the occurrence of secondary dilatation of the heart and the development of relative mitral insufficiency. The relief under these circumstances has been advanced as an argument in favor of the view that anginal pains are the result of increased intracardiac tension and muscle spasm. It may be, however, that breathlessness arising from

the cardiac dilatation in these cases compels the patient to restrict his exertions and to live at a level below which pain can be avoided. In the syphilitic form of the disease the outlook is more hopeful, although by no means wholly favorable. In some cases of syphilitic aortitis even the most energetic treatment is without avail. The prognosis, generally speaking, is most unfavorable in organic angina if the attacks occur during sleep or when the patient is quiet, or if pain is very easily provoked by exertion. Much depends, however, upon the effect of rest and the removal of secondary influences, such as excessive smoking, abuse of alcohol, or poisoning the result of local infection. If little or no improvement follows trea ment along these lines we must regard the condition as a very serious one. The occurrence of high blood-pressure during the paroxysms of angina does not make the outlook any worse, but persistent high tension between the attacks, especially if there is evidence of chronic nephritis, should make the prognosis guarded. The presence of valvular disease does not in itself materially increase the gravity of the prognosis, but, it is scarcely necessary to add, indications of muscular weakness make the outlook much more gloomy. The appearance of cardiac asthma is especially ominous.

The **treatment** of angina pectoris in the intervals between the paroxysms is for the most part that of the arterial or cardiac disease, of which the angina is only a symptom. Secondary influences, which may have been exhausting the heart itself or irritating the nerve-centers, should be sought for and removed. In all forms of the disease it is imperative that the patient should lead a quiet, easy life, should avoid as far as possible all mental and physical excitement, and should abstain from the use of tobacco and alcohol, and, as a rule, from that of coffee.

The element of rest is of vital importance in all cases, but good judgment is required in determining how complete it shall be and for what period of time the inactivity, relative or absolute, shall be enforced. If the attacks are frequent and easily provoked, or if there is much breathlessness, the patient should be advised to keep in bed. On the other hand, if the seizures do

not occur frequently or readily, and there are no indications of cardiac exhaustion, exercise need not be altogether foregone. Walking is the best form of exercise, but it should be on flat ground, and never against a strong wind. Gentle massage, and even a few passive movements, may sometimes be attempted, even in bedridden patients, but resistance exercises as well as the Nauheim baths are inappropriate. The use of the high-frequency current has been frequently recommended in hypertensive cases, but I have never found it very effectual.

The question of diet is scarcely less important than that of exercise. Small meals of readily digested food are to be recommended. Meat, as a rule, should be used sparingly. Hot breads, fried meats, greasy pastry, coarse vegetables, and highly seasoned dishes are inadmissible. The evening meal especially should be light. Muscular exercise and mental excitement of any kind after meals are particularly injurious. In the more severe cases with hypertension the Karell diet, carried out for a few days or a week at a time, often gives excellent results. Briefly stated, this consists in giving 200 c.c. of milk at intervals of four hours, from 8 o'clock in the morning until 8 o'clock in the evening. No other food or liquid is allowed. If there is much thirst the patient may be permitted to rinse out his mouth with water at intervals, and if hunger is urgent a small piece of dried toast may be given with each portion of milk. The Karell treatment is even more effective in some cases when preceded by blood-letting or wet-cupping. The bowels should be kept regularly open, mild aperients being used for the purpose if necessary.

Between attacks no drug is so generally useful as potassium iodid, although the manner of its action is not definitely known. It is most effective, of course, in cases of syphilitic origin, but it is not without a beneficial action in angina from other causes. However, in aged persons, in whom the cardiac pain is but one of the manifestations of the involutionary changes taking place in the arteries, the iodid, in my experience, is of little value. To be effectual in any case the drug must be given for a considerable period of time. Except in case of syphilis, doses of 10 grains

three times a day are usually sufficient. Next to the iodid, no remedy is so valuable as nitroglycerin. There is no positive proof that the relief it affords is due solely to a reduction of arterial tension; indeed, it often does good when the general blood-pressure is not high. It is perhaps useful chiefly by relaxing the coronary arteries, although by depressing the vagus it tends also to improve the tone and contractibility of the heart. Nitroglycerin and other vasodilators must be used with considerable judgment, however, in cases of chronic nephritis with hypertension. A too free use of such remedies in these cases is not rarely followed by dyspnea, anuria, and uremia. As a rule, far better results are secured from rest, a low diet, and purgation. Theobromin is a favorite drug with French clinicians. I have found it a valuable aid in some of the hypertensive cases. It acts especially well in connection with the Karell diet. The usual dose is 5 grains three times a day. The mixture of theobromin and sodium salicylate, known as diuretin, possesses no special advantages.

To guard against vagus inhibition, Allbutt speaks in the highest terms of atropin. He believes that it should be given systematically to every sufferer from angina. Personally, I have never obtained any very definite results from its use except, perhaps, in some of the more acute exacerbations of the disease. In the cases in which excessive nervous irritability is a conspicuous feature, bromids in full doses are indispensable. Digitalis has no place in the treatment of angina pectoris itself. It should be reserved for the menacing effects of cardiac dilatation. Alone or in association with theobromin it is also of service in cases of hypertension when the urine becomes scanty and uremia seems imminent. High arterial tension itself is no contraindication, for clinical experience has proved conclusively that no dangerous increase of blood-pressure ever results from its use in these cases. In anemic and debilitated patients tonics, especially arsenic and iron, are very useful.

Finally, any constitutional disease that may be present, such as gout or syphilis, must receive appropriate treatment. Salvarsan was formerly believed to be contraindicated in cardio-

vascular syphilis, but it is now known that if the drug is given at first in small doses (0.2 gm.), and the amount cautiously increased, it is safe and often of great value. Its use should always be followed by that of mercury and an iodid.

The Attack.—When the attacks are brought on by indigestion, they can frequently be staved off by the timely use of a brisk mercurial or saline laxative. Flatulency should be met by the administration of a stimulant carminative, such as whisky, aromatic spirit of ammonia, or spirit of ether, all of which act more quickly when taken in hot water. For the relief of the pain no drug is so useful as amyl nitrite. In the majority of cases a mere whiff of this speedily arrests the paroxysm. The patient should carry the remedy on his person in a small vial, or better, in the form of glass pearls, containing from 3 to 5 minims, which can be broken in a handkerchief and the vapor inhaled as soon as he perceives the pain. For mild attacks a drop of the spirit of nitroglycerin on the tongue is sometimes sufficient. When the paroxysms are severe and prolonged, morphin ($\frac{1}{4}$ to $\frac{1}{2}$ grain) and atropin ($\frac{1}{100}$ grain) should be given hypodermically. When amyl nitrite and morphin fail, recourse is sometimes had to inhalation of chloroform, but the use of this remedy is attended with a certain degree of risk. It is especially dangerous if the blood-pressure is low and symptoms of shock accompany the pain. The application of a mustard-plaster to the precordial region is sometimes useful in the cases in which the attacks are prolonged or occur in rapid succession. Cardiac depression following a paroxysm should be combated by such drugs as camphor, strychnin, and caffein, and, if necessary, by the inhalation of oxygen. After severe attacks it is necessary to enjoin absolute rest in bed for several days.

CLINIC OF DR. ROSS V. PATTERSON

JEFFERSON HOSPITAL

MECHANICAL DISORDERS AND IRREGULARITIES OF THE CARDIAC CONTRACTION

GENTLEMEN: I desire to invite your attention to some of the more important considerations regarding the various mechanical derangements and irregularities of the heart-beat, more or less commonly encountered in medical practice. It is my purpose particularly to point out to you important clinical diagnostic criteria by which each form may be recognized and differentiated from the others, as well as to indicate to you their significance and relative degrees of importance. I shall also very briefly discuss the treatment of each.

Taking a comprehensive survey of this entire group of affections, we find that, for all practical purposes, individual cases may be referred to one of the following seven categories:

(1) Sinus arhythmia.
(2) Heart-block.
(3) Premature contractions.
(4) Paroxysmal tachycardia.
(5) Auricular flutter.
(6) Auricular fibrillation.
(7) Pulsus alternans.

CASE I.—The young lad from the Out-Patient Dispensary is sixteen years of age. He is subject to asthmatic seizures, probably due to reflex irritation, the results of the excessive and untreated growth of adenoid tissue in the upper respiratory tract, is of neurotic constitution, and a cigarette habitué. As you observe from a general inspection, he is poorly developed physically. Upon routine examination, a well-marked irregularity of his heart has been noted. Careful study has established

an association between this irregularity and the respiratory movements, the pulse beating more quickly on inspiration and slower upon expiration, at the end of which the beats are relatively much more widely separated in time.

A history of repeated acute inflammatory involvement of the tonsils would justify a suspicion of pericardial or endocardial damage. Careful examination, however, reveals no signs of either; no evidence of enlargement of the heart, nor are there any symptoms of circulatory impairment other than we might expect to be associated with a frail constitution. The cold, moist hands are probably a vasomotor phenomena rather than the effect of a want of power on the part of the heart. The number of beats at the apex and at the wrist are the same, showing that each systole of the heart produces a pulse-wave at the wrist there is, therefore, no pulse deficit.

There is an entire absence of symptoms or signs of cardiac significance other than a rather marked irregularity having a relation to the respiratory movement. If we study this irregularity somewhat further, we find that all of the pulse-beats are of approximately equal strength; that the irregularity tends to be more marked after periods of rest, with a relatively slow cardiac rate; but, on the other hand, tends to be less marked, or to disappear, with increased cardiac rapidity due to emotion, exercise, or excitement. The irregularity is chiefly occasioned by variations in the length of diastole, so that the systoles, while equal in force, are irregularly spaced.

We have before us, therefore, a characteristic, well-marked example of sinus arhythmia, an irregularity probably caused by variations in the inhibitory influence exerted by the pneumogastric nerve, sharing in and affected by a functional instability of the nervous system, generally occurring at that period of life when the nervous system is most easily affected by emotional and other influences.

This is a form of irregularity the recognition of which is most important, in order that its true nature may be appreciated and its proper significance understood. Much needless concern, and even alarm, in the minds of both the laity and the

profession have been occasioned by this irregularity, and much unnecessary treatment instituted because of it. It is the most common form of arhythmia occurring in childhood and early adult life, hence the synonyms "juvenile" or "youthful arhythmia." It becomes progressively less frequent with advancing years, until in middle adult life it is comparatively infrequent, except among those of markedly unstable nervous systems; at a still more advanced period it is rarely encountered.

In itself it is not of unfavorable prognostic import, is not a sign of cardiac disease, nor does it result in cardiac damage or circulatory failure. In itself it requires no treatment. Not infrequently, however, as in the present case, it is associated

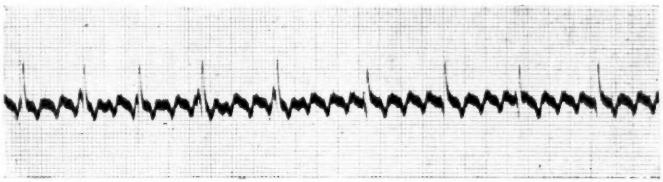

Fig. 24.—Sinus arhythmia. Electrocardiographic curve. Lead II. Each subdivision bounded by vertical lines equals 0.04 second. The complexes are all normal. The systoles are of equal duration. The irregularity is entirely occasioned by variations in the length of the diastolic periods. The rate averages 60. The cardiac cycle varies in length from 0.76 to 1.45 second.

with other conditions which demand energetic measures. It is probable that in the young lad before us much benefit to his general condition would result from the interdiction of the use of cigarettes; the removal, as far as is possible, of the sources of irritation in the upper respiratory tract; out-of-door life, good food, and freedom from causes of excitement; and that if improvement in his general and nervous condition be brought about, the cardiac irregularity would either disappear or be of very much less marked degree.

The electrocardiographic study (Fig. 24) to which I direct your attention shows the cardiac mechanism to be normal, with the exception of a variability in the length of diastole; the systoles are all of the same length and force.

CASE II.—The patient, H. G., male, age seventy-one, a gardener by occupation, came to the hospital complaining of shortness of breath and swelling of his legs. There are no family tendencies and he has never had a serious illness. He gives a negative history as regards venereal disease, rheumatism, or joint conditions. Does not use alcohol. Two weeks before admission he developed a cough attended with considerable expectoration, pains in the body, and shortness of breath. Swelling of the ankles appeared shortly thereafter. He felt weak and ill and took to his bed.

On admission there was considerable dyspnea, some cyanosis, but no definite jaundice. Thorax emphysematous in type. There were signs indicative of a moderate hydrothorax on the left side; breath sounds were harsh throughout, more so on the left side, with generalized musical râles.

The heart impulses are only slightly visible or palpable; heart sounds clear and distant; pulse 44 per minute, full and regular. The arteries exhibit an advanced degree of sclerosis. The edge of the liver in the right midclavicular line was 6 cm. below the costal margin. There was no evidence of ascites, but a considerable amount of edema of the legs. Six urine examinations showed findings all within the limits of normal, except for the constant findings of a trace of albumin.

During a period of four weeks the symptoms and acute signs which he exhibited upon admission have completely disappeared. The treatment has consisted of rest in bed, the use of vasodilators, and hydragogue cathartics. During this time his pulse has ranged in rate from 40 to 56, but is recorded in by far the greatest number of times at 44.

Discussion.—The clinical features of this case are, of course, quite ordinary, and exhibit the usual evidences of cardiac inadequacy and circulatory failure in an individual the subject of chronic myocarditis and advanced arterial sclerosis, occurring as primary conditions in a man of advanced years, of good habits, and a medical history singularly free from acute infections. The unusual feature of his case is, of course, a cardiac rate for the most part below 50, associated with acute symptoms of circula-

tory failure. The suspicion of some degree of heart-block is created by a ***heart rate*** of such ranges and occurring under such circumstances. In order accurately to ascertain the mechanism of the cardiac contraction careful polygraphic studies were made from time to time. A typical study is herewith presented to you (Fig. 25). The analysis shows complete dissociation between the auricles and ventricles, the relation between the auricular waves and those due to ventricular contraction in the venous pulse bearing no constant relation to each other. The diagnosis of complete heart-block can, therefore, be made with confidence, despite the lack of certain phenomena commonly associ-

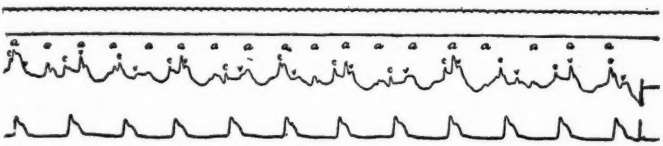

Fig. 25.—Complete heart-block. Each time division in this and subsequent tracings represents 0.2 second; the upper curve, venous pulse; lower curve, radial pulse. The whole period here shown covers sixteen seconds. The *c* and *v* waves of the venous pulse are the result of ventricular systoles; the *a* waves are caused by auricular contractions. The *c* and *v* (ventricular) waves bear a constant relation to each other. Studying carefully the relation of the *a* (auricular) waves to the *c* and *v* waves we find that almost every possible relation is shown (complete dissociation). The auricles and ventricles are pursuing independent, separate rhythms, both showing slight but independent irregularity. The auricular rate is 62.5; ventricular, 45.

ated with complete block. An unusual feature of his condition is a heart rate much beyond that usually found in complete block. Indeed, cardiac rates as low as 42 sometimes occur with a normal cardiac mechanism even in young people in the convalescence following the acute infectious fevers, and while the suspicion of a partial heart-block (usually a 2 to 1 rhythm) is justified, complete block usually produces a ventricular rate slightly over or under 30 per minute, owing, of course, to the well-known inherent tendency of the ventricle to generate its own stimuli for contraction at a much less frequent rate than the pace-maker, the more excitable, irritable portion of the heart, the auricle. The com-

paratively rapid rate of the ventricle in the present case doubtless accounts for the absence of syncopal and epileptiform seizures commonly associated with complete heart-block constituting the Adams-Stokes syndrome. Consideration of the history of the present case would justify the conclusion that the bundle of His is the seat of a primary sclerosis.

One more point as regards heart-block, well illustrated in the present case, and upon which I desire to lay emphasis, is the fact that heart-block is seldom a simple anatomic condition. Usually, even in those cases occurring at much earlier periods of life, there is associated myocarditis, often valvular damage, and progressive myocardial failure. We are too prone to regard heart-block as a condition in which the damage is restricted solely to the bundle of His. As a matter of fact, the bundle damage is usually but a part of the general cardiac degeneration, and to the latter is due the occurrence of the symptoms of circulatory failure.

In other words, heart-block (excluding the toxic cases) is generally but one expression of a wide-spread degeneration of the heart muscle. The unfavorable tendency is due, for the most part, to the myocardial degeneration rather than to the affection of the bundle. If heart-block were a question which solely concerned interference with the function of the bundle, the prognosis in these cases would be a favorable one. Restriction of the damage to the bundle doubtless accounts for the exceptional cases which have, without signs of circulatory failure, led active lives for periods of fifteen or twenty years. The prognosis, therefore, as in most cardiac conditions, is based upon an estimate of the general myocardial damage and the signs and progress of its degeneration, and its capacity to maintain the circulation under the unfavorable effects of an abnormal mechanism. The syncopal and epileptiform seizures are due to temporary ventricular silence—evidences of fatigue and incapacity of a damaged myocardium.

The treatment of these cases, like that of most other cardiac conditions, should be directed toward improvement and conservation of the myocardium. Digitalis is often of use, and may be used without hesitation in *complete* block. However, the

specific, depressive effect of digitalis upon the bundle may convert a partial block into a condition of complete block. Theoretically, atropin exalts the function of the bundle of His; practically, its use is without effect in the great majority of cases, probably owing to the marked damage already suffered by the bundle when the condition is first recognized.

In the present case we shall, of course, recommend the restriction of physical activities to within the limits of a much-damaged heart. Our patient will be told to live simply, exercise very moderately on the level, and, if possible, spend his remaining days in a rocking-chair on the porch or beside the fireside.

CASE III.—The man whom I next exhibit is fifty-six years of age. He presented himself to me several years ago, saying that he believed himself to be well in every particular with the exception of some trouble with his heart. This he describes as a disturbance in its rhythm, of which he is fully conscious, occurring more or less frequently. At times the disturbance occurs every few beats; at others, only a few times during the course of the day, more particularly in the evening after his day's work. At times he may go for several days with very little disturbance. The condition has been present for six or seven years, but has annoyed him more lately. He is a business man who takes a small amount of exercise, drinks moderately, and has had no serious illness for twenty years. There is an entire absence of any of the common, or even rare, causes of cardiac disease. He is an intelligent man, and his own observations with regard to his condition are both interesting and instructive. He describes the disturbance as one in which the heart seems briefly to stop; following which, with an unusual effort and with a very forcible beat, it resumes its regular rhythm. The disturbance is accompanied by a sense of alarm and "goneness," and when the disturbances are frequent the patient becomes more or less nervous and apprehensive. He has found that taking rather liberal drinks of brandy will cause the uncomfortable sensations to disappear; also the smoking of a considerable amount of strong tobacco. He notes, too, that he can "work the attacks off," as he says, by vigorous exercise. However, freedom lasts only

during the period of increased heart action attendant upon the effects of the tobacco, alcohol, or exercise; following these, when the heart rate slows, the disturbances are more frequent than before. He tells us, also, that during an attack of influenza which occurred during the winter, and in which there was a moderate degree of fever, he was entirely free of the condition during the febrile movement.

Our examination shows him to be of robust, rather well-developed build, indicating a man of vigor in apparent health. We

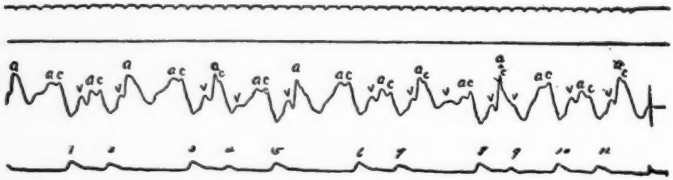

Fig. 26.—Ventricular premature contractions of frequent occurrence. Despite a high grade of irregularity, a tendency to rhythmic pulsation at the wrist (lower curve) will be observed. The 1, 2, 3, 5, 6, 7, 8, 10, and 11 pulse waves are the result of a normal mechanism; the 4 and 9 waves are premature; total failure of the ventricle to produce a wave at the wrist (pulse intermission) occurred after the 2, 5, 7, and 11 waves. The time occupied by a normal beat and an intermission is exactly equal to two normal pulse periods. There is a tendency, therefore, toward rhythm. The venous pulse (upper curve) shows the auricular contractions (*a* waves) occurring regularly without failure. The normal relation of the ventricular waves (*c* and *v*) to the auricular wave is deranged at the period of disturbance. The irregularity is occasioned, therefore, by a premature contraction of the ventricle occurring in advance of the arrival of the normal excitation wave from the auricle.

note a slight thickening of the arteries not greater than is frequent in a man of his years. Disregarding for the moment the disturbance in rhythm of the heart, we are unable to detect any abnormal physical signs. There are no signs of circulatory failure. The systolic blood-pressure is 150.

The cardiac disturbance, which is the sole important subjective and objective feature of his case, has been studied for several years. A single isolated disturbance may be described as follows: A heart and pulse, beating with absolute regularity and normal in character, are interrupted by what appears to be

at the wrist a complete failure of a pulse, *i. e.*, a "dropped beat." Auscultation at the apex simultaneously reveals a third sound occurring almost immediately after the second sound of the previous normal beat. This third sound, while of much less intensity, has the quality of the first sound, but is not followed by a second sound. It is, of course, due to a premature, feeble contraction of the ventricle of insufficient force to open the aortic valves; is followed by a prolonged period of silence, terminating in a beat of unusual force, producing a large pulse wave, and accompanied by exaggerated heart sounds, after which the heart resumes its normal rhythm. All of the disturbances are essentially of the same nature. The frequency varies at different times and under different circumstances. For periods of an hour or more the disturbance may replace every third or fourth beat, so that his pulse-waves at the wrist occur in groups of two or three (Fig. 26). At other times the disturbance has been at irregular intervals two or three times per minute.

Discussion.—We have here, of course, a marked example of premature contractions, or extrasystoles, with consciousness of the disturbance on the part of the patient. This is the most frequent form of cardiac irregularity which we encounter after fifty years of age in those without symptoms of circulatory failure. In many instances patients are totally unaware of the disturbance, and it is discovered upon routine examination by the physician. In still other cases the individuals may be conscious of the disturbance, but be free from any marked degree of apprehension. These disturbances are probably of both nervous and sclerotic origin. The premature beats are engendered by an irritable focus somewhere in the auricle, conducting system, or ventricle; and are, therefore, abnormal in their origin, in the contraction which results, and in their effect upon the pulse. They occur in hearts without signs of inadequacy or organic disease, as well as in advanced valvular disease with associated myocardial degeneration.

The tendency of practitioners is to overestimate the importance of this form of cardiac and pulse irregularity, although there is no doubt that in many cases they are one result

of extensive cardiac damage. In other cases they occur more or less regularly or irregularly over a period of years without associated signs or symptoms of cardiac damage; this latter group, in many cases, is probably nervous in origin.

Circulatory treatment, if required, is based upon the ordinary indications without regard to the extrasystoles. To regard extrasystoles as an indication of cardiac failure requiring the administration of cardiac stimulants is a therapeutic blunder which no language can be too vigorous to condemn. Their occurrences should, doubtless, create a watchful attitude on the part of the physician, and, if indications arise, the institution of such measures as will tend to conserve a myocardium somewhat more prone to exhibit damage than those not subject to this disorder. The only drugs which I have found to have the slightest value in relieving the mental alarm which sometimes attends the frequent occurrence of extrasystoles are the bromids. They have, of course, a very limited application and can be used only occasionally. Aside from this remedy, the regulation of the diet, habits, and mode of life of the individual may have some effect; not infrequently the occurrence of premature contractions may be made the lever whereby individuals may be induced to adopt a healthful régime which they would not otherwise be willing to embrace.

CASE IV.—The woman to whom I now direct your attention is forty-six years of age. She came to the hospital in the hope that, by a study of her case, we might be able to prevent recurrence of "attacks" similar to the one from which she is now suffering, and of which she has had many others during a period of years. She tells us that these attacks began twelve or more years ago. At first they occurred only once or twice a year. For the last five years they have been more frequent—every two or three weeks for a time—after which there have been periods of freedom for perhaps two or three months. Her last seizure occurred two months before admission to the hospital. She knows of no cause which brings them upon her. They have begun under a variety of circumstances, and in many cases have occurred spontaneously without apparent reason. One attack

seemed to be induced from straining at stool, the result of constipation; another began when she was sitting quietly sewing, without emotion or anxiety of any kind. Several have begun in her sleep. All of them have been of sudden, abrupt onset. The duration has varied from two to eleven days. Most of them last for four, five, or six days. The attack in which she was admitted to the hospital was of eleven days' duration, followed by an interval of three days, when a second one of six days occurred.

For the most part she has very little discomfort during these periods and often remains up and about. She once traveled from Philadelphia to Boston during one of them. Occasionally she has air-hunger, and in one instance this became urgent, and oxygen was administered for its relief. This was eight or nine years ago. Usually, however, she is fairly free from symptoms, but is mentally apprehensive, and during the intervals has lately become fearful of recurrences, and has refrained from more than moderate physical exertion in the hope that thereby she might avoid them. For the most part, however, she tells us that she is of a cheerful disposition and sanguine temperament. The attacks terminate as suddenly as they begin; the termination is always attended by a sensation similar to that which would be produced by striking her a sharp blow upon the chest with a mallet. If the termination of the seizure occurs during her sleep, the feeling of a blow awakens her. She is conscious of a very rapid action of her heart. The rate tends to be slightly more rapid at the beginning of a seizure, slowing slightly after several days' duration. Without feeling her pulse she is conscious of this slight slowing which she says has sometimes occurred. She is more conscious of the rapid heart action in the recumbent than in the erect position, and hence has usually remained up and about during the day. There is a desire for cold drinks, and she has a feeling of heat in the chest. She tells us that during the rapid action of her heart, position, exercise, emotion, or excitement will not in the slightest degree alter the rate of her heart-beat. This we have confirmed by our observations of her since she has been in the hospital. She has never had edema or any marked signs of circulatory failure.

Cardiographic studies made frequently during the period of rapid heart action exhibit a normal cardiac mechanism, beating regularly at the rate of 196 per minute (Fig. 27). Toward the end of the attack the rate reduced slightly to 180 per minute.

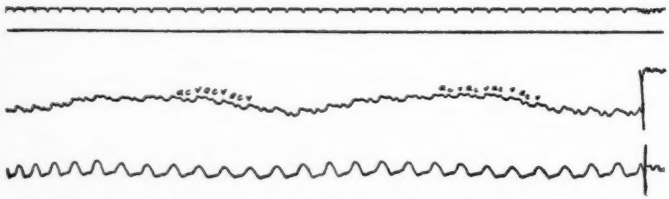

Fig. 27.—Simple paroxysmal tachycardia. The ordinary sequence of events in the cardiac mechanism is maintained. The ventricle responds regularly to each auricular contraction and their rates (196) are, therefore, equal. All the functions of the myocardium seem to be exalted. The interval which elapses between the beginning of auricular contraction and the beginning of ventricular contraction (*a–c* interval), indicating the rapidity of conduction of the stimulus wave from the auricle to the ventricle, over the bundle of His, is one-half (0.1 second) that of the normal period (0.2 second).

The termination was in the manner just described, after which the heart showed a rate of 80 per minute (Fig. 28). With the slow rate the usual influences of position, exercise, and emotion became evident.

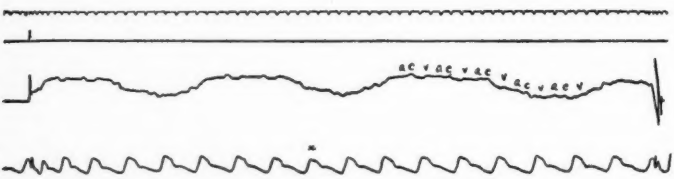

Fig. 28.—Tracings taken shortly after the termination of the tachycardia shown in Fig. 27. The mechanism is normal; the rate regular, 80 per minute. The *a–c* interval is 0.2 second. Occasionally a pulse wave is smaller (partial exhaustion of contractility), as at *x*.

The physical examination of her heart and circulatory system is otherwise without result.

Discussion.—We recognize here, of course, a case of simple paroxysmal tachycardia. The diagnosis is based upon the ab-

rupt onset and equally abrupt termination of the disturbance, the frequent recurrence of the condition, and the absence of other signs of cardiac disorder. An unusual feature of the case is a duration of eleven days. Attacks of simple paroxysmal tachycardia vary in duration from a few minutes to several days. The frequency of the seizures varies widely, from several attacks of short duration in a single day over a period of weeks, to other cases in which the attacks have been separated by periods of years; indeed, well-characterized cases have had but a single seizure.

The prognosis is variable. It is rather remarkable that, as in the present case, the heart is able to avoid exhaustion, beating at a very high rate for a long period of time. Some cases are attended with the signs of marked circulatory failure; with most alarming symptoms and with a fatal issue apparantly at hand, an abrupt termination has occurred with remarkable and prompt recovery—an important fact bearing upon the prognosis, making it obvious that in these cases unfavorable predictions should not be made with too great positiveness.

Various remedies and measures have been tried for the relief of the condition; none of them have been attended with any constant success. When we consider the spontaneous tendency to an abrupt termination, and the difficulty of knowing in advance when a given seizure will terminate, we realize that the administration of any remedy and the termination of an attack may be merely a coincidence, and have no relation as regards cause and effect. Right vagal pressure should be tried in every case; perhaps one-third of these cases are benefited thereby. The pressure, gently begun, should be continued to a degree sufficient to obliterate the carotid pulse wave in the neck. Faradization has occasionally been of benefit.

CASE V.—Our next patient, H. J. S., sixty years of age, a lawyer by occupation, has been under observation for the past four years. He tells us that he comes of good stock, has never had a serious illness, has always been well and strong, and lived an active, well-ordered life. He is a heavy eater and consumes large quantities of meat. He is a heavy smoker, but has never

used alcohol in any form. He is regular in his habits, takes a moderate amount of out-door exercise, and considered himself perfectly well until five years ago, when he began to have discomfort after eating, after exercise, and after periods of nervous stress and strain. He characterized his symptoms as being "attacks" lasting for a few minutes up to one-half hour, in which, sometimes with a feeling of slight nausea, there were pains beneath the sternum and in the left shoulder. Occasionally he had palpitation of the heart. His weight had fallen from 200 pounds, five years ago, to 150 at the time he first came under observation. He showed at that time marked tortuous pulsation of his brachial arteries; the peripheral arteries generally exhibited signs of diffuse thickening. There were signs of enlargement of the heart and a soft, systolic murmur at the apex. Systolic blood-pressure 195 mm. Hg.

Restrictions in his diet, limitation of his activities, and the use of nitrites and potassium iodid effected an improvement in his condition and a reduction of his blood-pressure to 165 mm. Hg.

He has been under observation at frequent intervals for the past four years. By the exercise of care in his diet, exercise, and the avoidance of emotional stress and overwork it has been found that he remains free from symptoms. Indiscretions of any kind, however, whether those attendant upon overexertion, excessive mental stress, or overeating, have resulted in a recurrence of his attacks of increasing intensity. At one time, while on a business trip attended with a good deal of physical and mental exertion, he developed a series of very alarming seizures in which the precordial pain was of intense degree, was referred to the shoulder and down the left arm, and attended by much mental perturbation and alarm. Repeated observations have appeared to establish a relation between increased blood tension and these alarming seizures of pain. After a number of demonstrations he has, with our help, learned a lesson from his experience, and has resigned himself to a life of very limited activity. For the past year he has been entirely free from symptoms, and has considered himself in good health. He frets a little at leading

the life of an old man, but is convinced that to attempt his former activities would be to court the return of symptoms of which he stands in great fear.

Discussion.—The diagnosis of angina pectoris in this case is unattended with difficulty or uncertainty. The anatomic diagnoses of general arteriosclerosis, hypertrophy, and degeneration of the heart, and especially with reference to his chief complaint, of sclerosis of the coronary artery, are also made without difficulty. The effect of extensive sclerosis of the coronary artery upon the circulation of the blood through it and its branches, and the consequent failure of nutrition of a myocardium much increased in bulk, already evidencing degeneration, struggling ade-

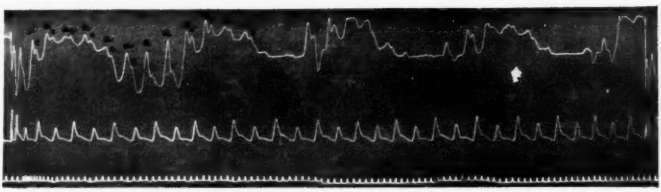

Fig. 29.—Pulsus alternans. The pulse waves at the wrist are absolutely regular as to sequence, but are alternately relatively large and small, indicating a partial failure of contractility each alternate beat. The *a–c* interval is 0.2 second (normal conductivity). The cardiac rate is 90; systoles 0.3 second; diastoles 0.4 second.

quately to maintain the systemic circulation despite (1) thick, non-resilient arteries, (2) increased peripheral resistance, and (3) a high blood-pressure, are all to be remembered.

An interesting observation with regard to his blood-pressure has been noted during the past year. It has been found in estimating the systolic pressure that if all the beats at the wrist disappeared with a pressure slightly beyond 195 mm. Hg., at a pressure of 195, only one-half of the beats "come through." In order that all of the beats may be felt the pressure must be lowered to 180. In other words, it would appear that half of his pulse-beats have a systolic pressure of 195 and the other half a pressure of 180, and that these beats, having different pressures, regularly alternate with each other. This variation

is not perceptible upon palpation, but by the use of the sphygmograph (Fig. 29) we are able to show that, although the pulse rhythm is perfectly regular, the beats are alternately relatively large and small.

We have in this case, therefore, an example of alternation of the pulse occurring in an individual in whom there can be no doubt as to the existence of extensive myocardial damage of a grave nature. Pulsus alternans is a sign of grave prognostic import occurring in individuals who have suffered extensive and serious myocardial damage from a variety of causes. The essential nature of its production is not well understood, but in its significance it leaves no room for doubt as a sign of ominous import. Its existence indicates a heart in which the margin of reserve is exhausted; a heart which is barely able to perform its function under even the most favorable conditions. For the most part it occurs in chronic myocardial conditions in which fibrofatty changes are extensive. Occasionally, however, we encounter it as a transitory acute condition. In this hospital we have a number of times observed it in pneumonia of the toxic type, in which the toxins seemed to exert a selective effect upon the heart. In those cases which have survived, the alternation has disappeared. We have also observed it in acute uremia and in acute lead-poisoning, in both of which conditions, with recovery, the alternation has disappeared. During its persistence, however, it is of serious significance, indicating an intense effect of acute poisons upon the heart.

The management of the chronic cases is, of course, obvious —the adoption of such measures as will tax a seriously damaged myocardium as little as possible, and the use of such remedies as will tend to relieve it of the burden of its work. While in no sense a specific, and of limited use, strychnin is a drug which offers more than almost any other at our command in most of these cases. The use of nux vomica in increasing doses until rather large amounts have been taken has apparently resulted in temporary improvement in some cases which could not be ascribed to any other agent. In the acute cases the treatment is, of course, directed to the primary cause, with a watchful eye con-

stantly directed toward the central organ of circulation, with due regard to those influences which, until recovery, will affect the heart unfavorably.

CASE VI.—S. S., age sixty, was admitted to the hospital complaining of shortness of breath and swelling of the feet and legs. On admission he told us that he had been well until four months ago. On careful inquiry, however, we learned that three years ago he had some swelling of his ankles and feet which lasted for a few days, and to which he attached no importance. The early symptoms of the present illness, beginning four months ago, were a slight nausea after meals and dizziness. He continued at his work, but four weeks later contracted a severe cold, and developed a racking cough with expectoration and pains in the chest, which compelled him to take to his bed. There were marked shortness of breath occurring in nocturnal paroxysms (pseudo-asthma), lasting for perhaps one-half hour, and sleeplessness. There developed almost immediately swelling of the feet. After two weeks in bed the symptoms subsided and he was able to resume his work, but he felt weak and ill, was short of breath, had swelling of his feet and ankles at the end of the day, and less frequent attacks of paroxysmal dyspnea. He was compelled to give up his work, and sought relief here in the hospital. On admission there were orthopnea, edema of the lower extremities and of the trunk. The chest is emphysematous in type. The lungs exhibited throughout diffuse mucous and submucous râles. The liver was enlarged, and extended three fingerbreadths below the costal margin in the midclavicular line. The superficial veins were enlarged, engorged, and he exhibited cyanosis of the tips of the toes, fingers, lips, and ears. The borders of precordial dulness were extended to the right and left. There is a double murmur at the aortic area and an absence of the aortic second sound. The arteries are visible, tortuous, thick, and may be rolled under the finger like whipcord beneath the skin. The pulse varies in rate over short periods of time from 90 to 110, and is slightly irregular as to sequence. Wassermann reaction is positive. During the past week there has been a marked improvement in his symptoms,

and he now feels able to leave the hospital, although considerable edema is still present. There seems little doubt that if he attempted to resume his work his symptoms would rapidly recur. At times the pulse-rate has increased to 145 per minute, but the patient himself has never been conscious of these attacks of tachycardia.

The treatment has consisted of absolute rest in bed, the liberal use of hydragogue cathartics, and 1 dram of tincture of digitalis per diem for five days, divided into three doses. Marked improvement has resulted from the treatment.

Discussion.—There is no difficulty in reaching an etiologic, anatomic, and functional diagnosis in this case. The signs point clearly to a double aortic valve lesion, general grave arteriosclerosis, chronic myocardial degeneration—all the effects of a luetic

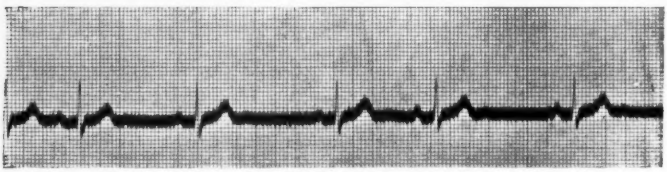

Fig. 30.—Auricular flutter. The curve presented is typical of this condition. Instrumental study is usually essential to a positive diagnosis.

infection superimposed upon a laborious occupation, the functional results being cardiac inadequacy, rupture of compensation, and circulatory failure. The diagnosis of the mechanical derangement of the heart is attended with difficulty. Only those intimately familiar with the derangements of the cardiac contraction would suspect the existence of auricular flutter in the present case, and even then only a provisional diagnosis is possible without the instrumental aid of either the polygraph or, still better, the electrocardiograph. The portion of the curve (Fig. 30) which I show you exhibits a regular auricular rate of 310 per minute. The ventricle responds to every third or fourth beat of the auricle. The time occupied by each ventricular cycle is, therefore, multiples of the time occupied by each auricular beat. The shorter pulse cycles, therefore, are exactly

three-fourths the length of the longer ones, occasioning a slight irregularity which easily escapes detection by ordinary methods of examination.

Auricular flutter is a comparatively rare condition, usually occurring in those at advanced periods of life who exhibit marked sclerotic changes, usually with associated degeneration of the heart muscle, and often attended with the signs of circulatory failure. Often the cases exhibit a rapid heart rate, persisting for a considerable period of time, sometimes for several weeks, and therein the condition differs from simple paroxysmal tachycardia. It also differs from the latter in an indefinite onset and a lack of consciousness of the rapid heart action on the part of the patient, such as is present in the former. Flutter may persist for months or even years, with the production of only slight symptoms; but sooner or later the signs of cardiac inadequacy develop. The ultimate prognosis depends upon the condition of the myocardium, and the success of treatment in correcting the abnormal mechanism. Treatment is often very satisfactory. Digitalis or allied drugs should be given in full doses. This is often followed not only by a prompt and remarkable relief of the symptoms supervening upon cardiac failure, but the mechanism of the heart is frequently restored to normal. Not infrequently, under digitalis, the flutter of the auricles is converted into fibrillation. This persists for a few days, and is accompanied by the grossly irregular pulse characteristic of that condition, succeeded, in turn, by a normal and regular rhythm. In our present case the administration of digitalis has evidently induced a partial block, so that the stimuli to contract are transmitted over the bundle only every third or fourth time. The clinical improvement, however, has been quite satisfactory.

CASE VII.—The next patient, F. B., male, sixty-four, was admitted to the hospital three days ago, complaining of general weakness, palpitation of his heart, and nervousness following an alcoholic debauch. He is obviously in a serious condition. His past history is rather ragged; he had pneumonia twenty years ago, has had repeated attacks of malaria, and several attacks of inflammatory joint trouble, which latter apparently was rheu-

matic fever. He has been a periodic drinker of whisky for many years. During the past two years he has been very short of breath on exertion and has often felt the beating of his heart. Blood spitting has occurred several times. He has been under medical treatment. Ten days ago he began to feel very much out of sorts and began to drink heavily night and day. Four days ago he had severe pain around the heart and distressing cough. Three days ago he was compelled to take to his bed; the following night, after a fall to the floor, he was brought to the hospital in the ambulance. On admission he was restless and mentally somewhat confused.

Physical examination shows slightly yellowed sclera, rounded thorax, with lessened expansion on the left, distinct dulness in the axilla, harsh breath sounds, slightly blowing in quality, but no râles. The right chest is hyperresonant and apparently clear. Heart examination shows diffuse visible impulse. Apex-beat, fifth interspace, 16 cm. from midsternal line. No shocks or thrills. The transverse limits of dulness in the fourth interspace extend from 3 cm. to the right of the midsternal line to 14 cm. to its left. There is a good deal of dulness over the manubrium and adjoining interspace. No murmurs have been detected. The heart rate is 160, pulse-rate 92, showing, therefore, a pulse deficit of 68 per minute. The heart action is exceedingly tumultuous and irregular. The pulse is most irregular as regards force, rate, and volume. The peripheral arteries exhibit the signs of advanced general sclerosis. Urine examinations indicate the presence of chronic diffuse nephritis.

The patient has been restless and confused since admission, but is fairly comfortable today.[1]

Discussion.—We are justified in assuming that the pathologic lesions, from which the present derangements are the

[1] The following day the respirations became increased in frequency, and the pulse became weak. There developed many crackling râles throughout the left axilla. Five or six hours later he became violent, and had to be forcibly restrained. Diffusible cardiac stimulants were without effect, and he died suddenly on the evening of the fourth day. The autopsy showed croupous consolidation of the base of the left lung; auricular dilatation of marked degree, chronic myocarditis, and diffuse nephritis. The valves showed no gross anatomic change.

outgrowth, had their beginning many years ago, and consist of general arteriosclerosis, chronic diffuse nephritis, and hypertrophy of the heart. Supervening upon the cardiac enlargement, myocardial degeneration has occurred with impairment of the power of his heart, until, under the influence of his habits and occupation, and with the progress of the lesions, a disproportion between the power of his heart and the work which it is called upon to do has been created. The circulatory symptoms which he now exhibits, constituting the clinical picture known as rupture of cardiac compensation, are the expressions of the disproportion created.

The anatomic conditions which he evidences, as well as the ordinary clinical symptoms which he exhibits, are quite ordinarily encountered and easily understood, so that, for the purpose of our present study, we may pass these by with but a cursory consideration.

I desire particularly to point out to you the association existing between the quite ordinary clinical features of his case and the mechanical derangements of his cardiac contractions and arterial pulse waves. The gross and wholly irregular character of both of these, as regards both force and sequence, is easily determined. We note, too, the total failure of many ventricular contractions to produce a pulse wave at the wrist, amounting to a failure, on the average, of 68 per minute (pulse deficit). Incidentally, this case illustrates a common clinical error of estimating the *heart-rate* by counting the *pulse-rate* at the wrist.

With all the facts before us, we need have no hesitation in including in our diagnoses auricular fibrillation. Examination of the graphic record (Fig. 31) confirms our observations with regard to the persistent and continuous irregularity of both the heart and pulse and the many incomplete systoles of the ventricle. The absence of auricular waves in the venous pulse indicates the absence of co-ordinate auricular contraction. The auricle is, doubtless, paralyzed and markedly overdistended, and gives rise to the abnormal degree of dulness previously noted over the base of the heart at the manubrium.

Auricular fibrillation is by far the most common form of cardiac irregularity in those with failing hearts, rupture of compensation, and circulatory insufficiency. It is a common condition in the medical wards of hospitals to which advanced cases of cardiac failure are admitted. No other mechanical derangement of the heart gives rise to such a marked degree of irregularity. Considered as a single clinical feature, it may be distinguished from all other forms of irregularity by an entire absence of rhythm, and an irregularity which increases with the rate of the heart.

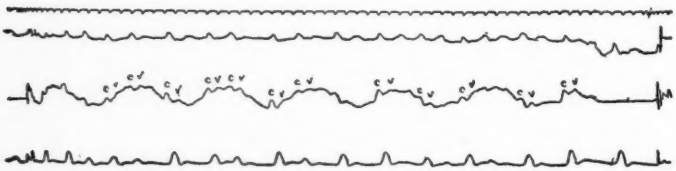

Fig. 31.—Auricular fibrillation. The cardiac contractions (shown in the upper tracing) and pulse waves are both wholly and continuously irregular. The number of beats at the apex is greater than the pulsations at the wrist. The complete absence of rhythm is the notable feature. The venous pulse shows complete absence of *a* (auricular) waves. The auricle has ceased to contract coördinately, and no longer acts as an efficient contracting chamber. The ventricle responds with irregular, rapid, haphazard, often incomplete contractions in response to the showers of stimuli transmitted to it from the contractions of individual fibers in the auricle.

As a general statement, it may be said that any irregular pulse of 120 or more is due to this condition. Sinus arhythmias and irregularity occasioned by premature contractions, aside from other differences which they exhibit and the conditions under which they occur, both tend to disappear entirely, certainly to become less marked, with a cardiac rate beyond 100.

Auricular fibrillation shows its greatest incidence in mitral stenosis; but it may occur, as in the present case, in the absence of any gross valve lesions. It is usually associated with an advanced degree of cardiac damage, and upon a badly damaged heart it imposes a serious additional burden. Considering all the circumstances under which it occurs, and the conditions

with which it is commonly associated, it is always of serious prognostic import. Once established, it tends to persist. Only occasionally is the normal mechanism resumed. It carries with it in heart conditions a significance of sinister import. A study of a large number of cases shows few with a duration of life beyond three years after the inception by the heart of this abnormal rhythm, even with symptoms of a relatively moderate degree of intensity.

This is the condition in which digitalis exhibits its most favorable effects, and upon which it chiefly depends for its well-deserved reputation. It is in this condition that digitalis has gained its reputation for slowing the heart, an effect chiefly achieved by depressing the function of the conduction system, and inducing a partial degree of heart-block, so that the multitudinous, irregular, and haphazard impulses which originate in the auricle are in part prevented from passing over the bundle. With the slowing of the ventricles the pulse deficit tends to disappear and the pulse to become more regular, but even with the most favorable results close attention will detect an irregularity even in digitalized hearts beating at rates of 60 or lower. The sudden fatal termination of some of these cases, under digitalis administration, is probably to be accounted for by the induction of a complete heart-block. A reduction of the rate to within normal limits, even in the absence of untoward symptoms of digitalis administration, indicates withdrawal or a marked reduction in digitalis dosage.

CLINIC OF DR. MARTIN E. REHFUSS

JEFFERSON HOSPITAL

GASTRIC INFECTION

MODERN medicine attempts as far as possible to determine facts, and to establish by means of various procedures the existence or non-existence of various pathologic conditions. It is only when definite points cannot be established that we are privileged to wander in the realm of theory and hypothesis. Today I wish to speak of a condition which has passed from the field of speculation to that of an established fact; that is to say, actual infection of the gastric walls in such a manner as to constitute true gastric infection. We are truly committed to the principle of isolated or focal infection of most of the organs of the body, but the stomach has been one of the organs to be included rather late. The reason is not far to seek, inasmuch as this organ has a number of protective barriers which render it exceedingly difficult for such infection to occur.

There are four reasons why the stomach normally resists infection:

(1) The acid secretion, which is inhibitory, if not actually destructive, to bacterial growth.

(2) A thin, mucoid protection to the mucous membrane which serves as a barrier against infection.

(3) The fact that the organ in health is constantly shifting its contents, so that the introduction of infected material fails to gain a foothold on the gastric wall.

(4) The excessive vascularity of the gastric wall, with its cavity, giving an efficient drainage on all occasions.

A little reflection will readily emphasize the importance of the above factors, inasmuch as a destruction of or diminution in these factors is the principal medium responsible for infec-

tion. But infection occurs not merely by mouth, but in all probability the most likely route of infection is by way of the

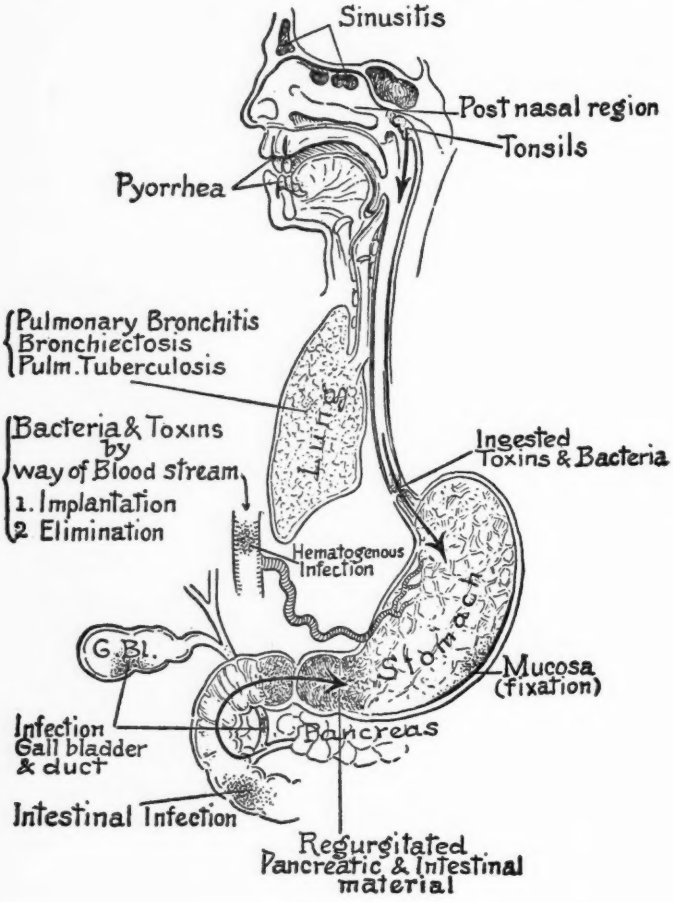

Fig. 32.

blood-stream, namely, hematogenous infection. The work of Richet in France and Rosenow in this country makes this possibility exceedingly likely, although I am far from convinced

of the infective nature of gastric ulcer. There can be no doubt, however, that there is not only a selective localization of pathologic organisms, such as has been pointed out by Rosenow, some being implanted on the colon, others in the appendix, others in the gall-bladder and gastric wall, but there seems to be also, according to the work of Richet, a selective elimination of micro-organisms, some of them being eliminated on different levels throughout the gastro-intestinal tract, and not a few, such as the typhoid bacillus, for instance, even seeking elimination through the gastric walls.

In other words, infection must occur either by way of the mouth (per oram) or by way of the blood-stream. The former is hardly possible in health, but if we have a breaking down of the normal barriers, this becomes possible, as I shall attempt to demonstrate. Probably the most important single condition which is conducive to infection is the reduction or disappearance of gastric acidity. We have been able to show that there is, even in the interdigestive intervals, a definite secretion which is physiologically active. If, associated with this, there is a disturbance in motility and degeneration of the gastric walls through inflammation, such as Hayem and others have indicated, all the conditions for gastric infection are present. In other cases the hematogenous infection is unquestionably the explanation.

How, then, are we to diagnose this condition? The following case illustrates exactly what I mean, and indicates the method which I have employed in demonstrating infection of the stomach.

Mr. H. D., admitted to hospital suffering principally from distress in the epigastrium. His chief complaints are swollen feet and distention and belching after eating, but no actual pain and no nausea and no vomiting. He has lost 25 pounds in the last year. His appetite has fallen off, and he has become obstinately constipated. No jaundice; no cyanosis. For the past fifteen months he has had a purplish discoloration of the arms and legs and pain in the elbows, back, and both feet, and in the last few weeks a diffuse purpuric eruption. Previous history negative, with the exception of measles and scarlet fever in infancy, and typhoid fever at the age of seventeen.

Examination disclosed two important points, namely, a more or less generalized purpura, particularly severe in the lower extremities, and a general localized tenderness in the epigastrium, not confined to any one point and unassociated with muscular rigidity. There are many points regarding this case which are of interest, just as there are many points, too numerous to mention, regarding a whole series of these cases, which I have collected. Time only permits me to point out, however, the important points in this case and the reasons why the inference of gastric infection is justifiable.

A study of the stomach reveals the following facts: Examination of the empty stomach reveals blood, many bacteria, some pus; no food retention and no hypersecretion, but an excess of gastric mucus. The stomach is cleansed by lavage and then the patient is given a test-meal—the conventional Ewald meal in this instance—and the entire cycle of gastric digestion studied. Notice that on physical examination there is no evidence of a mass, no sharply localized tenderness, no enlargement of any of the abdominal organs, no evidence of peritoneal irritation or inflammation. Fractional analysis reveals the following interesting and important points:

GASTRIC ANALYSIS

Residuum: Pus, blood, mucus, bacteria.

Time.	T. A.	F. A.	Mucus.	Blood.	Bacteria.	
¼	3.0	0	"	"	"	
½	5.5	0	"	"	"	
¾	7.0	0	"	"	"	
1	8.0	0	"	"	"	Gram. Neg. Bac.
1¼	11.0	0	"	"	"	
1½	14.1	0	"	"	"	
1¾	11.9	0	"	"	"	

Feces—occult blood.

R. B. C.	4,030,000
Poly.	62
W. B. C.	8,800
Lymph.	34
H. B.	62
L. L.	3 per cent.
Bas.	1 "

There is a total achylia; not the spurious type, but a total achylia through the entire phase of gastric digestion. There is no free acidity, no pepsin formation, and milk will not curdle. Notice, too, that in this instance these specimens are tinged with fresh blood already laked or hemolyzed. This is unusual. The normal individual and most pathologic cases never show the red specimens we see here. Even when hemorrhage occurs, there may be shreds or clots—rarely hemolyzed blood. Furthermore, the possibility of trauma through the tube rarely produces more than an occult bleeding or minute flakes of fresh blood, and if the technic is correct this should not occur. In this instance, however, the blood is frankly pathologic, and to my way of thinking indicates an unusually irritable mucosa. I have seen identically the same findings in another case of purpura, and these findings lead me to believe that in such disease the bleeding is not merely subcutaneous, but also mucosal in certain portions of the gastro-intestinal tract. But most important to my mind is the fact *that all the fractional specimens, without exception, contain large numbers of bacteria;* and second, *that these bacteria are practically identical, and in this case is a Gram-negative, non-motile bacillus.* This is never seen normally, and is readily recognizable under the moderately high powers of the microscope, such as $\frac{1}{6}$-inch objective, and does not require an oil-immersion objective to demonstrate the organisms. Normally, and even pathologically, in other conditions than this, with the exception of bacteria in the residuum, organisms are exceedingly infrequent, and never persistent and constant such as seen in the above case. Even after gastric lavage these same organisms are found. This constitutes the first clue to infection. It might be argued that the food introduced is not sterile, but in the thousands of examinations that I have made the picture which I am describing as characteristic of gastric infection is not seen in other conditions. The persistence of the presence of organisms in different samples, the similarity in the nature of the organisms in each instance, the presence of the organism after lavage, and the presence of evidence indicating direct mucosal disturbances, seems to me to indict the stomach as the primary or, more probably, secondary

focus of infection. But that is not all; destruction of the gastric infection by two means (1, direct disinfection and irrigation; 2, by vaccines from the stomach) results in the cases I have been able to study and observe carefully in a disappearance of the condition.

In my series there were two cases of purpura—one case of a staphylococcus infection, apparently as far as I could find confined to the stomach, several private cases, one of which was treated by vaccines, and in which, as near as we could determine, there was a primary bronchiectasis and a secondary gastric infection with the Micrococcus catarrhalis as agent; several cases in which the organism isolated resembled the colon bacillus, and one case secondary to a mixed pulmonary infection. The interesting and important point regarding these cases, all of which were associated with either achylia or pronounced subacidity, was the most important and essential fact that in all cases the above *evidences of gastric infection were found*, and, second, *in all cases a cure was only brought about by direct gastric treatment.*

This idea of gastric infection is by no means new. Many observers have pointed out infection in the stomach principally under the heading of ulcer or erosion. Probably in these cases erosion accounts for the frequent presence of blood. Bottcher, Dieulafoy, Widal and Meslay, Letulle, Chantemesse, Bezancon, Gandy, Griffon, and others have produced gastric lesions by means of bacteria. Jenson, Brunner, Dugeon, Sargent, and Loepar have isolated organisms from lesions, principally ulcerations. The staphylococcus, streptococcus, pneumococcus, and colon bacillus seem to be the chief offenders, although in some of our cases these organisms were not so sharply defined or there was secondary infection. Richet pointed out the elimination of certain organisms like the typhoid bacillus on a level with the stomach.

One other point. These findings may be confused with the picture of the condition described by Pilcher as achlorhydria, but that condition was based on the single gastric examination according to the old method, which, in my judgment, does not inculpate the stomach as the direct focus of infection. This is

extremely likely, but the interpretation is not such. It is my belief that most of those cases are, in reality, cases of infected gastritis with either primary or secondary infection of the gastric mucous membrane, and the statement of that author that they are usually associated with infection of the gall-bladder or the appendix, and clear up after the offending member is removed, is not the case in severe gastric infections. I am inclined to think, however, that in many of those cases there was a primary hematogenous infection from some local point elsewhere, with secondary infection of the gall-bladder or appendix and the stomach. One of the striking points which the fractional tube reveals is the presence of pus in the stomach residuum (empty stomach). This might be intragastric true pus from the gastric wall (apart from phlegmonous gastritis), or may be extragastric pus appearing in the stomach after ingestion. I have tried to make a differentiation by the character. In the gastric type the pus is usually purée of leukocytes intimately mixed with the gastric contents, while in the extragastric or ingested varieties the material is more discrete—in shreds or strands—and has a tendency, owing to its frequent admixture with air, to float on the surface. This pus is seen in cases of sinusitis, tonsillitis, pyorrhea, and in the whole line of bronchial and respiratory infections, particularly in the various forms of bronchitis and pulmonary tuberculosis. The diagram indicates the possibilities in that direction, and I am inclined to believe that in not a few cases the result on the stomach is not merely through the blood-stream (toxemia and direct hematogenous infection), but also from the presence of swallowed infected material. Just how this mechanism acts is not quite clear, although the lack of the normal acidity and a delay in motor-tone are the predominating factors in bringing about infection.

Diagnosis is then made not merely on the presence of pus, blood, and bacteria in the empty stomach, but the *constant presence of these factors throughout the entire cycle of digestion, coupled with one or more of the factors mentioned above.* A microscopic examination of several or all of the samples is desirable in cases where the possibility of infection is entertained.

What is the significance of this condition? In all the cases which I have observed the general health has been more or less compromised. Some of these cases exhibited profound anemia and even cachexia resembling that of neoplasm. Not infrequently the gastric picture is that of neoplasm, with certain points lacking, and the differential diagnosis of neoplasm, as from infected gastritis, is sustained by the subsequent course of the case. In 2 cases the deterioration in general health and weight was as great as that of neoplasm. One point must be remembered, and that is, the *association of secondary gastric infection with gastric carcinoma*—a point which must always be borne in mind.

Most important in these cases is the associated intestinal and not infrequently hepatopancreatic disturbances, shown by the character of the movement. The danger of intestinal infection is always possible, and the differentiation between primary gastric infection and a secondary gastric infection due to regurgitation of infected material from the intestinal tract presents occasionally a nice problem for solution.

In the discussion of the treatment, the fractional tube not merely lends itself to a diagnosis of this condition, but it paves the way for a rational treatment. If there is infection, two means suggest themselves—the use of direct disinfection and the isolation of the causative organism and the preparation and administration of a vaccine. I have used both of these methods, and in practically every case I resort to the first method. On a few occasions I have had vaccines prepared. In one case—that due to a catarrhal (*catarrhalis*) infection—the effect was most striking and happy. The method of gastric disinfection is as follows: The fractional tube is passed into the empty stomach and the entire residuum removed. The stomach is then irrigated with an alkaline solution of bicarbonate of soda or a weak solution of the various alkaline antiseptics, such as liquor antisepticus alkalinus, and finally by distilled water. This is followed by the direct instillation of the disinfectant into the stomach through the tube. For that purpose I have used nitrate of silver, the colloidal iodid of silver, argyrol, and protargol, as well as hydrogen peroxid. The first two have commended themselves to me, and I do not

hesitate to use in excess of the therapeutic dose well diluted—for instance, ½ gr. of nitrate of silver in several ounces of water, allowing the solution to remain five or ten minutes in the stomach, after which I aspirate part of the solution introduced and allow the rest to remain and exercise a continued action in the stomach. I have used the larger doses, but on two occasions the passage of this substance into the intestine induced cramps. The method given above is absolutely safe and is often followed by pronounced results not merely in the gastric findings, but in the general symptomatology accompanying the infection. I would direct attention to these methods, inasmuch as I think we are destined to see a change in the treatment of various gastric conditions by the use of direct treatment, such as the specialist uses in the treatment of mucous membranes elsewhere in the body. This subject is capable of much greater development, and I have only hinted at the possibilities in its study.

CLINIC OF DR. JUDSON DALAND

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ULCERATIVE ENDOCARDITIS, SECONDARY TO DENTAL SEPSIS, TREATED BY AUTOGENOUS VACCINE

CASE I.—This man, aged forty-three years, entered the hospital complaining of weakness, mental depression, fear of crowds, tremor, irritability, epigastric distress with distention, attacks of fever at intervals of from ten to fourteen days, and a loss of 30 pounds. These symptoms began six months ago. The family and the previous medical history are unimportant. At the age of twenty-five years he had typhoid pneumonia, confining him to bed for ten weeks, from which he made a good recovery. The right patella was fractured at the age of thirty-seven years, and after operation a good recovery was secured, but he remained nervous and emaciated.

From the age of thirty-eight to forty-two years he had recurring headaches at intervals of two or three weeks, ultimately relieved by the correction of astigmatism. Two years ago he became easily exhausted, nervous, excited when meeting strangers, began to lose weight, complained of indigestion, and these symptoms continued for one year, but he recovered under forced feeding. Six months ago an attack of sore throat, chilliness, fever, bodily pains, and prostration was diagnosed la grippe and confined him to bed for ten days, and was followed by edema of the ankles and inability to walk more than two or three blocks without exhaustion. The ankles remained swollen ever since, and at intervals of about two weeks attacks of chills, fever, and sweat occurred, lasting two or three days, and in the interval he stated that fever is absent. About three months ago his physicians were unable to find any evidence of disease of the kidney, malaria,

syphilis, or tuberculosis. A murmur was discovered thirteen years ago by his brother, who is a physician, but at no time were there any cardiac symptoms, although he has lived at an elevation of 6000 feet and was occasionally at an elevation of 9000 feet. Prior to two years ago he averaged four or five glasses of whisky, two or three glasses of beer, ten cigarettes, and two or three cigars daily; food habits good, occupation healthful, suffered no mental or physical stress or strain, and denied having had syphilis or gonorrhea. One year ago his weight was 158 pounds and a few days ago it was 122 pounds, a loss of 36 pounds.

The recurring attacks of chills, fever, and sweats led one of his physicians to diagnose malaria, but no malarial parasites could be discovered in the blood. The suspicion of tuberculosis was strong, but no sign of this disease could be detected. Another physician erroneously diagnosed laryngeal tuberculosis. Although symptoms existed for six or more months, no diagnosis had been made.

Physical examination showed well-marked emaciation, weakness, marked pulsations in the neck; the apex-beat was below the left nipple, between the fifth and sixth interspaces, and occupied an area larger than normal, and the area of cardiac dulness was increased. In recumbency a well-marked systolic thrill was felt over the apex, and auscultation revealed a loud systolic murmur which was transmitted from the apex to the angle of the left scapula and the manubrium, but no murmur was heard in the carotids. There was well-marked sclerosis of the radial and temporal arteries and the abdominal aorta pulsated violently. The pulse was accelerated and occasionally intermittent. The heart was regular in force and rhythm and pericardial friction-sounds were absent. In the sitting posture the pusle was 132, the systolic pressure was 125 mm., and the diastolic pressure 80 mm. In recumbency the pulse was 124, the systolic pressure 135 mm., and the diastolic pressure 76 mm., and after exercise the pulse was 140, the systolic pressure 140 mm., and the diastolic pressure 80 mm. With the exception of feeble vesicular breathing the lungs were normal. A well-marked gastric splash was elicited three hours after breakfast, indicating food stagnation. Palpation caused

hyperperistaltic movements of the intestines. There was a well-marked varicocele on the left side and slight enlargement of the middle lobe of the prostate, but no evidence of disease of the seminal vesicles.

The upper left premolar and first molar and the upper right molar were capped. Absence of teeth on the right side prevented good mastication.

Re-examination the following day gave the same results, and the fluoroscope showed pylorospasm, intestinal hyperperistalsis, ptosis of the cecum, hepatic flexure, and transverse colon. The heart shadow extended further to the left than normal and was enlarged.

Numerous urinalyses showed the continuous presence of a trace of albumin, cylindroids, hyaline and granular casts, and frequently erythrocytes.

Examination of the blood showed no malarial parasites, the erythrocytes were 76 per cent., hemoglobin 60 per cent., and the leukocytes 13,200 at 10.30 A. M. Polymorphonuclear leukocytes 90 per cent., large lymphocytes 0.2 per cent., small lymphocytes 9.6 per cent., basophils 0.2 per cent. One month later the erythrocytes were 56 per cent., the hemoglobin 48 per cent., and the leukocytes 12,000.

The amount of gastric contents removed one hour after a test-breakfast was larger than normal and contained a trace of lactic acid, but was otherwise normal. Physical and blood examinations excluded tuberculosis, malaria, and syphilis. The Wassermann reaction was usually negative, but was occasionally weak or moderately positive. Two carefully made cultures of the blood, made upon several different media, gave negative results. You will observe that the temperature is recorded for the past four months, that the periods of fever to which the patient refers represent rises from 102° to 104° F., the maximum occurring at 3, 6, or 9 P. M., and in a few hours descends to 96° or 97° F. Temperatures above 103° F. were usually accompanied by chills and sweat. When the temperature arose to 100° F. there was no chill, sense of fever or sweat, and, therefore, the patient erroneously believed that no

fever existed. A study of the temperature-chart shows that the fever was typically intermittent. As collections of pus, malaria, tuberculosis, and other diseases producing intermittent fever were excluded, search was made for a focus of infection, but none could be found in the tonsils, sinuses, including the middle ear and mastoid, the prostate, seminal vesicles, appendix, gall-bladder, gall-ducts, lungs, and pleuræ. A roentgenogram revealed periapical abscesses at the roots of the left lower pre- and first molar and upper left second bicuspid. Exploration showed that the upper left second bicuspid contained cotton, offensive in odor. The pulp canal was enlarged, and two sterile broaches were passed into the periapical spaces and a non-hemolyzing streptococcus obtained of low virulency, 1 c.c. of the bouillon culture did not kill a white mouse in twenty-four hours. This streptococcus did not ferment inulin, and from it a vaccine was made. The infected teeth were extracted and the sockets cureted. The equivalent of 500,000,000 of the organisms was injected at intervals of five days, later increased to 750,000,000, and toward the end gradually decreased to 150,000,000. The leukocytes were increased 1000 after one injection of the vaccine; the larger doses caused depression. The vaccine treatment was continued for two months and exerted no beneficial effects upon the fever or symptoms. Later the patient gradually grew weaker; the leukocytosis disappeared, a splenic infarct, hypostatic congestion, and edema of the lungs preceded death, which occurred about nine months after the initial symptoms and three months after he came under observation. Permission for an autopsy was declined.

This patient had mitral valvulitis prior to thirteen years ago due to an unknown cause. It probably occurred at the age of twenty-five years, when he had an alleged typhoid pneumonia, although it may have been due to a forgotten attack of tonsillitis. Originally, the patient probably possessed low resistance, which is suggested by the continuation of nervousness and loss of weight after the operation upon the fractured patella, the marked disturbance of the nervous system caused by astigmatism, and the attack of nervous exhaustion two years ago.

The beginning of this fatal illness, erroneously ascribed to la grippe, was due to septic ulcerative endocarditis involving the previously diseased mitral valves, secondary to streptococcus infection from the tonsils or roots of the teeth, or both. The discovery of putrescent material in the cotton that filled the root canal and streptococci in the periapical space suggests that this infection was primary by the way of the pulp canal. When periapical abscess occurs in a normal tooth it is usually secondary to a focus elsewhere in the mouth or body, if not infected by contiguity from an adjacent tooth. That complete compensation had been secured from the original endocarditis is evidenced by the absence for many years of cardiovascular symptoms, even though exposed to the circulatory strain of living at 6000 feet. The occurrence of exhaustion from walking two or three blocks with edema of the ankles, tachycardia, and increase in pulse-pressure were due to decompensation. The attacks of chills, fever, and sweat were due to the direct entrance into the circulating blood of streptococci and their toxins from the ulcerated mitral valves; the vascular sclerosis was largely the result of secondary septic endocarditis. The abnormal increase in amount of normal gastric juice recovered one hour after a test-breakfast, and the presence of a gastric splash three hours after breakfast were probably due to pylorospasm. The pylorospasm and intestinal hyperperistalsis were probably toxic in origin; the ptosis of the large intestine was probably largely due to atony of the muscular walls of the abdomen, secondary to streptococcus infection; the nephritis, progressive chloro-anemia, and polymorphonuclear leukocytosis were secondary to the streptococcus infection; the splenic infarct was due to an embolus, probably originating in the diseased mitral valves. The hypostatic congestion and edema of the lungs were a terminal manifestation of cardiac decompensation.

Although well-marked clinical evidence that infective organisms existed in the circulating blood, repeated cultures upon different media revealed no organisms. The vaccine made from the organisms discovered in the periapical space of the infected tooth may not have represented the organism or the particular

strain that existed in the ulcerated mitral leaflets. The large doses of vaccine did harm by causing increased weakness. A leukocyte count immediately before and one hour after injecting a moderate dose of the vaccine showed an increase of 1000 leukocytes per cubic centimeter.

The occasional weakly positive Wassermann reaction was probably due to changes in the serum secondary to streptococcus infection.

As a rule, ulcerative endocarditis is not diagnosed until after it has existed for from three to six months; in this case the physicians were deceived by ascribing the cardiac signs to the mitral valvulitis known to have existed years before the present illness.

Clinically, in this part of the world, fever, usually intermittent, that continues for more than two months without obvious cause is often due to ulcerative endocarditis, and may exist in the absence of a cardiac murmur, or the murmur may be scarcely audible and may intermittently disappear. In this case, where the diagnosis was in doubt, the existence of an increase in the cardiac rate out of proportion to the fever was a sign of diagnostic importance. I recall no case of septic ulcerative endocarditis that had not *already* existed for at least four or five months, and in a rather large consulting experience fail to recall a case where the family physician had made a positive diagnosis. The disease is usually erroneously diagnosed as influenza, typhoid or paratyphoid, tuberculosis, or malaria.

After septic ulcerative endocarditis has existed for several months the secondary changes affecting vital structures are so extensive that recovery is almost impossible, and all cases that have come under my observation terminated fatally. The hope of the future lies in the *early* diagnosis, the scientific employment of a vaccine made by a skilled bacteriologist from microorganisms recovered from the circulating blood, and the removal of a focus of infection when present.

CASE II.—Male, aged forty-one. At the age of eighteen years he had an attack of acute articular rheumatism complicated by mitral valvulitis, from which he recovered without

decompensation. At the age of twenty years he contracted a gonorrheal urethritis, resulting in stricture, that was apparently cured. During the past three or four years an abscess existed about the apex of the right upper first bicuspid. In August, 1916, a roentgenogram revealed a periapical abscess from which pus was discharged by a fistula in July; an enlarged left ventricle of the heart; a dilated arch of the aorta the walls of which showed several calcareous plaques and considerable congestion of the bases of both lungs, but no evidence of disease of the appendix or gall-bladder.

In March, 1917, he began to complain of feeling tired and of aching pains in the legs. In the latter part of June marked night-sweats occurred, with fever, loss of weight, anorexia, and increased pulse-rate. Hemoglobin was 55 per cent., leukocytes 10,000. On August 19th weakness compelled the patient to remain in bed. Temperature observations, begun on August 20th, showed a subnormal temperature in the morning with an evening rise to 101° F. The night-sweats gradually disappeared, but the temperature-curve remained unchanged until about September 4th, when for ten days, with one exception, the evening temperature was below 100° F. Thereafter the typical intermittent fever continued. Weakness increased, albuminuria occurred, and septic phlebitis developed in the right saphenous vein. When first seen, September 28th, in consultation with Dr. F. G. Runyeon, to whom I am indebted for bedside notes and report of autopsy, physical examination revealed weakness, emaciation, anemia, hypertrophy, and dilatation of the left ventricle with mitral regurgitation, aortic obstruction, and regurgitation, enlarged liver and spleen, and typical intermittent fever.

On October 4th a pure culture of the Streptococcus hemolyticus was obtained from the blood from which a vaccine was made. The first dose was 90,000,000, the second 180,000,000, and after each injection there was a marked rise in temperature, so that the third dose was reduced to 60,000,000. Subsequently, the doses were gradually increased to 180,000,000, but no benefit was observed and the disease steadily progressed.

On November 9th a sharp, stabbing pain occurred at the level of the sixth rib, at the left side of the chest anteriorly and laterally, due to a pulmonary infarct, which exerted no effect upon the fever.

On November 20th death occurred, preceded by orthopnea, cyanosis, and moderate edema of the feet.

Necropsy revealed extensive ulceration of the posterior leaflet of the mitral valve, which looked as though it had been nibbled away by a mouse. Many chordæ tendinæ had been ulcerated and others were broken. The aortic leaflets near the coronary artery showed ulceration and a tumor formation about the size of the distal half of the distal phalanx of an adult's thumb. The ulceration extended into the aorta, almost perforating the wall, and also into the right auricle. Only a thin partition existed between the base of the ulcer and the right auricle, so that the fingers almost came in contact. The remaining aortic valves were thickened, sclerotic, retracted, and one of them showed a hard ridge-like thickening of the edge. There was a whitish plaque upon the surface of the left auricle, near the mitral opening, measuring 1 by ¾ inch, ovoidal in shape, and a similar plaque in the arch of the aorta, the walls of which were thick and rigid. There was well-marked dilatation and hypertrophy of the left ventricle of the heart; diffused bronchitis with areas of pulmonic consolidation; the lower lobe of the left lung contained a wedge-shaped infarct; the liver was greatly enlarged, and extended downward to the transverse umbilical line; the consistency was increased, and section showed evidence of chronic parenchymatous inflammation; the gall-bladder was normal; the consistency of the spleen was increased, its size doubled, and there was a thrombus in the right saphenous vein.

This is a typical case of septic ulcerative endocarditis, involving the mitral and aortic leaflets, and it is probable that in March or earlier these diseased valves became infected with the Streptococcus hemolyticus from abscesses at the roots of certain teeth. The vaccine treatment was begun soon after the disease was recognized and produced no beneficial effect.

In this case a pure culture of the Streptococcus hemolyticus was obtained from the peripheral blood, and, therefore, the vaccine was worthy of full confidence, but as the disease had existed for approximately six or seven months the secondary changes in the various important tissues of the body and loss of resistance were probably sufficient to prevent recovery, in addition to the fact that the original focus of infection in the root of a bicuspid tooth, although under the care of a dentist, was not rendered aseptic, as was proved by the appearance of an abscess in this region a few days before death.

In combating this disease the original focus should be removed whenever possible before employing an autogenous vaccine.

CASE III.—Male, aged forty-six years, admitted to the hospital on March 21, 1917, complaining of weakness, chills, fever, and sweats. The family history was negative. He had been in the habit of gunning on the Eastern Shore of Maryland in a swampy territory where mosquitoes were plentiful. Chews and smokes about 1½ ounces of tobacco daily.

In January he observed gradually increasing weakness, attacks of chilliness, followed by fever and profuse perspiration. On March 2d he was admitted to a hospital in Philadelphia, where he remained until March 21st, during which time the morning temperature was normal or subnormal, the evening temperature 102° or 103° F., accompanied by chilliness and sweats. On admission to this hospital on March 21st he presented but few symptoms. He was obviously weak and became dyspneic on slight exertion and was febrile. These three symptoms were apparently unnoticed by the patient, who was somewhat apathetic, somnolent, and mentally sluggish. The skin was markedly pallid, moist, and clammy. Bright red ecchymotic spots, varying in size from a pin-head to a pea, were distributed over the neck, trunk, and extremities. The conjunctivæ were pale and there were several small subconjunctival hemorrhages on the left lower lid. The corneæ were bluish white and glistening. The pupils were moderately contracted, but reacted normally. The mucous membrane of the mouth was pale.

The teeth were apparently in good condition. Slight absorption was noted about the roots of the lower central incisors, but no pus was found in these regions. The tongue was dry, somewhat brown, and protruded without tremor in the median line. The tonsils were not diseased. There was no adenopathy. Physical examination of the lungs was negative. The veins, more especially the jugulars, were overdistended. The apex-beat of the heart was in the fifth interspace in the midclavicular line. The area of cardiac dulness was increased to the left. The muscular element of the first sound at the apex was fair, but occasionally a reduplication of the first sound was audible. No murmurs were heard upon admission, but later a faint systolic murmur developed in the mitral area. The aortic second sound was accentuated and the radial, brachial, and temporal arteries were sclerosed and tortuous. For a few days there was stiffness and soreness of the joints, especially the wrists. The musculature was flaccid, but the abdominal wall was tense, partly from tympanitis, which interfered with the examination of the abdominal contents. The liver and spleen were slightly enlarged; the kidneys were not palpable, and no tenderness could be elicited anywhere in the abdomen, even on deep pressure. The knee-jerks were normal and there was no Babinski or ankle-clonus. Hearing impaired, probably due to inattention, as examination showed no abnormality; ophthalmoscopic examination practically negative. The fever gradually diminished, and from April 1st to 6th the maximum evening temperature was 100° F. or less. The systolic blood-pressure in recumbency was 130 mm., the diastolic pressure was 80 mm., the pulse-pressure 50 mm., and the pulse 90 per minute. The Wassermann reaction was negative.

Examination of the blood on March 26th revealed 48 per cent. erythrocytes, 42 per cent. hemoglobin, and 9600 leukocytes; 57.5 per cent. polymorphonuclears, 34.5 per cent. small lymphocytes, 7.5 per cent. large lymphocytes, 1 per cent. basophils, and 0.5 per cent. mast cells. On the 5th of April the leukocytes were 13,000 and on the 12th of April there were 11,200 leukocytes, 68.5 per cent. were polymorphonuclears, 27 per cent. small

lymphocytes, 4.5 per cent. large lymphocytes, and later the leukocytes numbered 7200. Blood-culture very active.

Examination of the feces was negative. Several urinalyses showed a faint trace of albumin, with numerous hyaline and granular casts, many pus-cells, and a few erythrocytes. Moderate renal inadequacy was shown by the phenolsulphonephthalein test. The excretion was 19 per cent. the first hour and 23 per cent. the second hour, and practically the same results were secured two weeks later.

The hebetude, somnolence, weakness, chills, fever, and sweat, in conjunction with the fact that the patient was frequently bitten by mosquitoes while gunning in swampy regions along the Eastern Shore of Maryland, aroused the suspicion of the attending physician that malaria existed, but repeated examinations of the blood failed to disclose the parasite. There was no evidence of pulmonary tuberculosis, the Von Pirquet test was negative, and no symptom or sign of intestinal tuberculosis or typhoid fever could be elicited. Upon the supposition that the symptom complex was due to a latent septic focus and in the absence of any obvious collection of pus, an examination of the middle ear, mastoid, and sinuses was made, with negative results, with the exception of a small amount of pus in the left maxillary sinus in association with a deviated septum. A small amount of pus in the urine was attributed to chronic posterior urethritis, but no suppurative seminal vesiculitis or prostatitis could be discovered nor any infection of the appendix or gall-bladder. Despite the fact that the teeth showed no evidence of disease, and there was an absence of large fillings, capped teeth, and bridges, a roentgenogram showed an abscess of the posterior root of the right upper second molar, and the adjoining molar was unerupted and appeared rudimentary. On April 6th the infected molar was removed under novocain anesthesia, and considerable pus escaped from the gum around this tooth during the injection of novocain. Fever, leukocytosis, and polyarthritis disappeared and the patient showed symptomatic improvement, so that although the prolonged, irregular, and intermittent fever and the later development of a faint, mitral systolic murmur and

numerous ecchymotic spots, varying in size from that of a pinhead to a pea, over the neck, trunk, extremities, and left conjunctiva, interpreted as septic emboli, pointed toward ulcerative endocarditis, the hope was entertained that the septicemia was secondary to the periapical abscess. The left ventricular hypertrophy was supposed to be largely secondary to advanced arterial sclerosis, which in turn was believed to be caused by heavy lifting, chronic tobacco poisoning, and septic endarteritis; and the feebleness of the circulation, as shown by the physical examination, was corroborated by the low diastolic and large pulse pressure. The albuminuria, cylindruria, and erythrocytes indicated a mild grade of septic nephritis, and the anemia, leukocytosis, mental hebetude, enlarged liver and spleen were also due to sepsis. The severity of the anemia was an index of the severity of the infection. The pulse-rate continued in its normal relationship to the temperature, whereas, usually, it is disproportionately increased. The first differential leukocyte count showed an increase in lymphocytic increase, which is not unusual in systemic infection following focal infection. The patient was so much improved that he returned home on May 16th. His attending physician, Dr. Ludwig Loeb, informed me that later the fever returned, that he rapidly grew worse, and died on May 28th.

Autopsy revealed an enlarged, pale, flabby heart, and the left ventricle contained a chicken-fat clot. The thickened mitral leaflets showed calcareous deposits and vegetations resembling a cauliflower growth involving the aortic valves. The walls of the arch of the aorta contained patches of atheroma especially noticeable around the orifices of the coronary arteries. The kidneys showed chronic parenchymatous nephritis; the spleen was much enlarged in all diameters and contained an organized infarct the size of a lime. The bladder showed cystitis.

The marked though temporary improvement following the extraction of the infected tooth suggests that greater benefit may have been secured if it had been removed earlier; on the other hand, the periapical abscess may have been secondary and not primary, as the tooth showed no evidence of previous disease.

CONTRIBUTION OF DR. JOHN A. KOLMER

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THE DIAGNOSTIC VALUE OF EXAMINATIONS OF CEREBROSPINAL FLUID[1]

The Origin of the Cerebrospinal Fluid in Relation to Pathologic Changes in Cerebrospinal Diseases. Spinal Puncture for the Purpose of Securing Cerebrospinal Fluid for Diagnostic Purposes. The Diagnostic Value of Observations Upon the Pressure and Physical Appearance of Cerebrospinal Fluid. The Diagnostic Value of Chemical Examinations of the Cerebrospinal Fluid. The Diagnostic Value of Cytologic Examinations of the Cerebrospinal Fluid. The Diagnostic Value of Bacteriologic Examinations of the Cerebrospinal Fluid. The Diagnostic Value of Immunologic Examinations of the Cerebrospinal Fluid. Specificity of the Wassermann Reaction. Diagnostic Value of the Wassermann Reaction in Syphilis of the Cerebrospinal System. The Wassermann Reaction and Its Relation to Treatment. Conclusions.

WHILE the cerebrospinal fluid has been for some time the subject of much research and many philosophic discussions among anatomists and physiologists, it is only recently, indeed, only since Quincke's epoch-making introduction of lumbar puncture in 1891, that the clinical importance and value of spinal puncture and an examination of cerebrospinal fluid has been recognized.

Since that time the usefulness of these procedures in the diagnosis of various pathologic conditions of the cerebrospinal system has been constantly enlarging, and the union between clinic and laboratory has become closer and closer, due to elaboration from time to time of delicate tests and reactions for the detection of pathologic changes in the fluid. We need no longer base our conclusions upon one or two observations on the condition of the fluid, but rather upon the data obtained through various

[1] From the McManes Laboratory of Experimental Pathology of the University of Pennsylvania, Philadelphia.

physical, chemical, bacteriologic, and serologic tests. Indeed, with few exceptions the diagnostic value of cerebrospinal fluid examinations is only appreciated after fairly complete studies, the total results being considered with the clinical manifestations of disease.

For example, a condition of the cerebrospinal fluid characterized by yellow color called "xanthochromia," great excess of protein, and spontaneous coagulation of the fluid in the test-tube, with slight or no increase of cells, is known as "massive coagulation and xanthochromia" or the "syndrome of Froin," and is due to pressure and a space-resisting process with localized stasis of the fluid somewhere along the spinal meninges. If, in addition to the symptoms of this compression syndrome, serologic examination reveals a positive Wassermann reaction, or bacteriologic tests demonstrate one of the micro-organisms common to a purulent meningitis, or the tubercle bacillus, then the exact nature of the space-resisting process is at once evident.

At the present time, therefore, spinal puncture and the examination of fluid have ceased to be subjects merely of academic interest and speculative theorizing, and have become of very practical moment to the clinician in the diagnosis of diseases of the nervous system and in the treatment of various infectious conditions, and to the surgeon in his attempts to deal more successfully with the problems of cranial and spinal surgery. It is apparent, however, that in order to understand and interpret aright the many pathologic changes in the fluid which may be revealed by various tests and reactions, the physician should have a clear concept of the cerebrospinal fluid under normal conditions and its physical, chemical, and cytologic characteristics; indeed, it is only by a careful comparison of the normal and the abnormal fluid that we finally arrive at a true understanding of many pathologic processes of the cerebrospinal system.

It is well known that discernible changes in the cerebrospinal fluid do not occur with all diseases of the cerebrospinal system, despite the severity of the symptoms which they produce; on the other hand, certain other diseases, and particularly the various forms of meningitis, may produce early and profound changes

from the normal. It is my purpose at this time to make brief inquiry into the fundamental principles concerned in the alterations of the chemistry, cytology, and immunology of the cerebrospinal fluid in diseases of the cerebrospinal system, and to discuss these changes in relation to the diagnostic value of lumbar puncture and laboratory analysis of the cerebrospinal fluid.

THE ORIGIN OF THE CEREBROSPINAL FLUID IN RELATION TO PATHOLOGIC CHANGES IN CEREBROSPINAL DISEASES

Without detailing the large amount of experimental work conducted on the subject of the origin of the cerebrospinal fluid by Dixon and Halliburton, Frazier, Plaut, Weed, Dandy and Blackfan, and numerous other investigators, the preponderance of evidence indicates that *normally* the cerebrospinal fluid is for the most part a secretory product of the choroid plexus, but that some is derived from the blood-vessels of the nervous tissues and possibly also from the pituitary and pineal glands. It bears a very close resemblance to the perilymph of the internal ear and the aqueous humor of the eye, but differs greatly from the fluids of other serous cavities and the plasma of the blood. Owing to the fact, therefore, that normally the cerebrospinal fluid is largely a secretory product of the choroid plexus and other glandular tissues, or, at least, that these tissues exercise considerable influence upon the properties of the fluid, it is unusual for one to find in the normal cerebrospinal fluid the natural antibodies and other substances so easily demonstrated on the blood-serum as natural diphtheria antitoxin, hemolysins, complements, and anaphylactic antibodies. During disease in which the cerebrospinal system, and particularly the choroid plexus, remain intact, the cerebrospinal fluid maintains its normal characteristics; bacteria and antibodies may be present in the blood and even in the fluid of other serous cavities without finding entrance to the cerebrospinal fluid. For this reason, an examination of the cerebrospinal fluid is of no value in the diagnosis of general infections without definite involvement of the tissues of the cerebrospinal system. The choroid plexus is to be regarded as the main guardian against infection, although its defensive powers

are easily disturbed, as shown by the experiments of Flexner and Amoss, in which the intraspinal injection of sterile horse-serum or even simple spinal puncture, accompanied by some loss of blood, were sufficient to greatly reduce the resistance of the tissues to infection with poliomyelitis virus.

After microparasites have gained access to the cerebrospinal tissues with the production of inflammatory changes, the cerebrospinal fluid undergoes certain changes, due to the extravasation of blood elements from the engorged vessels of the inflammatory tissues into the fluid, and possibly to some influence upon the choroid plexus, altering the properties of its secretion and power of selective filtration. In this manner well-marked changes may occur in the fluid in interstitial infections, as acute anterior poliomyelitis; surface infections of the meninges or other lesions, like tumors, involving the meninges induce more extensive changes in the fluid than deeper seated lesions.

In other words, deep-seated lesions of the tissues of the brain and spinal cord, as the various degenerations of important nerve tracts and small, deep-seated tumors, produce slight or no discernible alterations in the fluid as long as the normal sources of the fluid remain intact; just as soon, however, as the lesion is of such a character as to involve the surface of these organs and the meninges with congestion of the blood-vessels, with probable interference with the circulation of the fluid and its absorption, serous and cellular elements gain access to the fluid and change its characters in a more or less definite manner.

SPINAL PUNCTURE FOR THE PURPOSE OF SECURING CEREBROSPINAL FLUID FOR DIAGNOSTIC PURPOSES

The very large number of spinal punctures which have been made by many physicians the world over indicates that the operation itself, when properly conducted in the lumbar region with a suitable needle and under aseptic conditions, is quite without danger; the pain produced during the operation can also be largely removed by preliminary infiltration of the tissues, along the passage the needle is to take, with 0.5 to 1 c.c. of a sterile 1 per cent. solution of eucain. Careful preparation and selection

of the spot for puncture, with arching of the back to widen the intervertebral spaces, a knowledge of the direction the needle should take, according to the position of the patient, and avoiding undue force which may injure bone or even break the needle, are requisties for uniform success in conducting lumbar puncture. Regardless of the amount of experience the physician may have, each operation should be conducted with deliberation and gentleness and with an effort to limit pain; even the most expert may fail in this relatively simple operation and failure is caused usually by haste and overconfidence.

For diagnostic purposes 3 to 4 c.c. of fluid are ample for all ordinary tests, including the Wassermann reaction. When the latter test is not required, 2 c.c. should be sufficient. These amounts of fluid may be removed from the average adult person without harm, but it is good practice to have the patient rest quietly and in the prone position for an hour or two after the puncture, to lessen the tendency to aching of the head and nausea which may follow.

In the various forms of meningitis, when the fluid is under pressure, larger amounts of fluid may be withdrawn and with considerable temporary relief of the symptoms.

While realizing the great value that an examination of the cerebrospinal fluid may have in the diagnosis of incipient or advanced disease of the cerebrospinal system, and particularly the Wassermann and colloidal gold tests in syphilitic infection of these tissues, I regard lumbar puncture of sufficient surgical importance to require due deliberation on the part of the physician before subjecting his patient to the ordeal, and am opposed to its promiscuous and hasty performance. This is particularly true, since lumbar puncture alone may so disturb the choroid plexus or other mechanism of defence of these tissues against infection as to favor infection if certain microparasites are in the blood, or so situated as to gain ready access to these tissues. Flexner and Amoss have demonstrated this fact in experimental poliomyelitis in monkeys, and similar experiments with the tubercle and influenza bacilli, pneumococcus, and meningococcus should be conducted to determine if similar conditions hold in

these infections. Since lumbar puncture may, therefore, favor infection of the meninges and cord in poliomyelitis, the physician may have ample reason for hesitating to perform the operation; least harm is likely to follow if the operation is done skilfully and without drawing blood; most harm may follow a clumsy operation and the injection of various substances which are irritants and have no demonstrable parasiticidal influence. Moreover, the injurious effects of lumbar puncture appear to be overcome or neutralized by the prompt injection into the subarachnoid space of immune serum, which, in poliomyelitis, is to be obtained from convalescents; it would appear, therefore, that if anterior poliomyelitis or meningococcus meningitis are suspected, two infections which may be treated successfully with immune sera, and particularly the latter, the cerebrospinal fluid should be examined without delay and the serum promptly administered.

These remarks are not intended to discourage the practice of lumbar puncture among general practitioners, and particularly so since these physicians are usually first to be consulted; indeed, it is more likely that the average physician will delay lumbar puncture too long. My sole object is to draw attention to the fact that the recent work in poliomyelitis may have an important general bearing upon lumbar puncture in acute infections, and to draw due attention to the possible dangers of the operation. In chronic infections, and notably syphilis, lumbar puncture may not produce harm, although it is conceivable that the activity of spirochetes may be increased, and particularly by the intraspinal injection of irritant substances possessing no demonstrable spirocheticidal properties. Unfortunately, a Wassermann test with the blood-serum of a person with syphilitic involvement of the cerebrospinal tissues and cranial nerves may not react positively, whereas the test conducted with the cerebrospinal fluid may; for this reason a negative blood Wassermann test may prove misleading, and justifies the physician in advising lumbar puncture for diagnostic purposes. Moreover, as pointed out by Fordyce, the colloidal gold-test with cerebrospinal fluid may yield the first definite information on an incipient paresis.

The possible harmful effects of lumbar puncture in syphilis of the nervous system consequent to a lowering of local resistance may be overcome by the prompt administration of salvarsan by intravenous and intraspinous injection, and a positive Wassermann in the presence of clinical symptoms should be regarded as indicating active antiluetic treatment.

It appears to me that lumbar puncture for cerebrospinal fluid for the purpose of laboratory examination is correctly practised by those physicians who bear in mind the value such an examination may possess in the diagnosis of certain diseases of the cerebrospinal system; who are on the alert for the detection of symptoms and signs indicating the involvement of these tissues, and who then proceed to conduct the operation with due deliberation and aseptic care, and with measures to limit pain and even the slight shock which may accompany or follow the operation among older children and adults who are not acutely ill. In addition, the physician should be ready to promptly administer by intraspinal injection such known specific remedial measures as antimeningococcus and anti-influenzal serums, poliomyelitis immune serum, and tetanus antitoxin if the corresponding infection is found to be present.

The following precautions should be observed in collecting cerebrospinal fluid for laboratory examination:

1. The fluid should be collected in two small sterile test-tubes in order to separate the first flow, which may be tinged with blood, from the pure fluid. The tubes should be numbered 1 and 2; the fluid in No. 1 is not necessarily wasted by the presence of a few erythrocytes, as it may be used for the Wassermann reaction after removing the erythrocytes by centrifuging, whereas the pure fluid is necessary for the chemical, cytologic, and colloidal gold-tests. Graduated centrifuge tubes are particularly serviceable, as the amount of fluid drawn may be measured during the operation.

2. The fluid should be examined as soon as possible after withdrawal. Indeed, the total cell-count should be made at the bedside unless the laboratory is close at hand. Cultures should be made first and before chances for contamination are magnified by other tests and the micro-organisms die off.

THE DIAGNOSTIC VALUE OF OBSERVATIONS UPON THE PRESSURE AND PHYSICAL APPEARANCE OF CEREBROSPINAL FLUID

Pressure.—While the problems associated with pressure of the cerebrospinal fluid need much further study under normal and various pathologic conditions before the full practical value of pressure readings will be known, there is sufficient data at hand indicating the diagnostic value of this procedure in certain diseases of the cerebrospinal system.

It has been proved that the pressure of the cerebrospinal fluid varies directly with the pressure of the venous sinuses and is practically identical with it. The pressure oscillates with coughing, crying, forced respiration, and muscular movements; the position of the patient exerts a very marked influence, the pressure being four or five times higher when the patient is sitting up than when in the prone position on the left side. In children, according to Quincke, the normal and pathologic cerebrospinal pressure is about one-third less than in adults. At the present time, however, it is extremely difficult to draw any deductions from the variations in cerebrospinal pressure, partly because there is no standard instrument for measuring it, and partly because of the variation in pressure under normal conditions. It is necessary for us to adopt a standard instrument and a standard technic in order to secure results of value. At the present time I am of the opinion that the mercury manometer and technic of Landon fulfil these requirements, and I would urge physicians to adopt both. The instrument is very simple and convenient and yields sharp readings. With the adult patient on the left side and quiet, the normal reading varies from 6 to 10 mm. of mercury, with an average nearer 8 mm. (Landon). Readings even slightly above 12 mm., under proper attention to details of the technic, are regarded as suspicious, while readings of 20 mm. or higher are distinctly pathologic.

Increased pressure is found especially in acute and chronic meningitis, and particularly in the acute forms due to the meningococcus, tubercle bacillus, and poliomyelitis virus; in paresis, cerebral and spinal tumors, traumatic and also idiopathic epilepsy, congenital and acquired hydrocephalus, and in some

cases of cerebral injury. As far as I am aware, the pressure alone is not pathognomonic of any one condition, but the information of a correctly taken cerebrospinal fluid pressure is to be interpreted with the results of laboratory analysis of the fluid and clinical signs and symptoms. This subject constitutes a wide and fertile field for future investigation, employing a standard instrument and a rigid and uniform technic, particularly with regard to the normal pressure at different ages, from children to adults, and in the study of not only direct spinal and cranial conditions, but intoxications accompanied by delirium, as in eclampsia, uremia, alcoholism, and acute infectious fevers.

Physical Examination of Cerebrospinal Fluid.—Valuable information is frequently obtained by close inspection of cerebrospinal fluid. The normal fluid is limpid, colorless, sparkling, perfectly clear, odorless, and does not coagulate. A cloudy fluid, varying from the faint ground-glass opacity of the fluid in acute poliomyelitis, which may be appreciated only after viewing the fluid in a test-tube held against a black background, to the distinctly turbid and puriform fluid of meningococcus and pneumococcus meningitis, is to be interpreted as pathologic, and is usually found in the various types of acute and chronic meningitis of microbic origin due to the presence of leukocytes, endothelial cells, bacteria, and other inflammatory products.

However, a perfectly colorless and normal-like fluid may be found in tuberculous meningitis and the earliest stages of other forms, such as poliomyelitis, as well as in various chronic lesions of the brain and cord. In tuberculous meningitis and acute poliomyelitis, however, the amount and pressure of the fluid will be increased, and chemical and cytologic examinations will furnish further data differentiating the fluid from the normal.

In severe icterus the cerebrospinal fluid may become discolored, but in practically all other instances a change in the color of the fluid is due to local conditions in the cerebrospinal system itself. The fluid collected from below spinal tumors and other space-constricting lesions may show a deep yellow color (xanthochromia), with spontaneous coagulation upon standing, due to the presence of blood-pigment and a great excess of protein. In

cerebral hemorrhage or other hemorrhagic conditions, where the blood is not in direct contact with the subarachnoid space, the hemoglobin may cause color changes while blood-cells are absent. At first the fluid has a slight yellow color; in a few weeks the color deepens to a brownish yellow and gradually returns to the normal colorless fluid.

Blood may gain access to the fluid as the result of trauma during lumbar puncture; in such instances the first flow is deeply tinged, followed by pure spinal fluid. When the fluid is first clear and then bloody, hemorrhage from the subarachnoid space, as in injuries of the skull and vertebral column, is to be suspected. In severe infections accompanied by erosion of small vessels the fluid may contain small amounts of blood, and this is especially likely in acute poliomyelitis due to the action of the virus upon the intimal lining of blood-vessels.

THE DIAGNOSTIC VALUE OF CHEMICAL EXAMINATIONS OF THE CEREBROSPINAL FLUID

The chemistry of both the organic and inorganic constituents of the cerebrospinal fluid is quite complex, and, owing to the difficulty of securing large amounts by spinal puncture, practical chemical methods for diagnostic purposes are usually confined to examinations for protein, dextrose, and chlorids. Investigations bearing on the mineral constituents, organic acids, and fatty substances have been made with interesting and instructive results, but they demonstrate little of practical value, owing chiefly to difficulties in technic and securing sufficient amounts of undiluted and suitable fluid.

By far the major portion of normal cerebrospinal fluid is water; in 1000 parts about 990 parts are water and 10 are solids. The total quantity of protein is about 0.02 to 0.03 per cent., or 0.2 to 0.3 gram per 1000 c.c. The substance found in normal fluid capable of reducing copper, and first described by Deschamp and Bussy in 1852, has been quite conclusively identified as dextrose; the amount in the cerebrospinal fluid is slightly less than that found in the blood, and averages, according to Mestrezat, from 0.048 to 0.058 per cent. or 0.48 to 0.58 gram per

1000 c.c. Sodium chlorid constitutes the chief salt, being present in 0.725 to 0.750 per cent.

Protein.—There is considerable discrepancy in the reports of various investigators regarding the identity of the protein found in normal cerebrospinal fluid. Thus, certain persons regard the protein as serum albumin, others as serum globulin, or a mixture of globulin and albumose; there is a need of further research in this subject employing more delicate methods; but, bearing in mind that the normal fluid is probably the result of selective transudation or filtration from the serum of the blood in addition to a true secretion from the cells of the choroid plexus, it appears to me advisable to side with those who regard the protein as a mixture of albumin and globulin, the latter predominating in proportion of about 1 to 3. At any rate, the protein of the cerebrospinal fluid is usually increased in organic diseases and injuries of the brain and spinal cord, and the detection of this increase is more important than exact quantitative differentiation of the various proteins.

A well-marked increase of the protein in the fluid is always pathologic, and usually indicates an inflammation of either infectious or toxic origin involving the meninges, plexus, or substance of the brain or cord, and accompanied by congestion, infiltration, and exudation of serum and cells. Probably in the majority of instances the protein is derived primarily from the blood-serum, either by direct transudation or through some disturbance of the function of the mechanism of selective filtration ascribed to the choroid plexus, as mere hypersecretion of the plexus alone is not likely to produce a fluid containing an increase of protein. The congested area surrounding a tumor or injury may result in the transudation of protein constituents from the blood to the cerebrospinal fluid, and, if the circulation of the fluid is interfered with, the protein content may be very high, as in the "syndrome of Froin," characterized by a yellow fluid very rich in protein and undergoing spontaneous coagulation in the test-tube.

In all instances an acute inflammation shows a greater protein increase than chronic inflammation. Next to typical

fluids of xanthochromia and massive coagulation, the largest amounts of protein are to be found in surface infections of the meninges, as the meningitides due to the meningococcus, pneumococcus, streptococcus, tubercle, and influenza bacilli. In acute anterior poliomyelitis the inflammation is primarily an interstitial meningitis rather than a surface infection, and, accordingly, we do not usually find as large amounts of protein in the cerebrospinal fluid. In cerebrospinal syphilis, tabes dorsalis, and paresis the protein is usually increased.

While the amount of protein in the fluid bears a close relationship with the severity of the infection, a normal protein content does not in itself indicate a normal condition of the central nervous system. Thus, normal values may be found in the early stages of acute anterior poliomyelitis and in such conditions as multiple sclerosis, epilepsy, and brain tumors unaccompanied by meningeal irritation; also in non-organic psychoses and in general infections, such as typhoid fever, pneumonia, and gastrointestinal disturbances of infants with acute meningeal irritation or the so-called "serous meningitis," or meningismus with hyperproduction of cerebrospinal fluid of practically normal constitution. Therefore, while an increase of protein indicates organic and pathologic changes, the absence of protein increase does not exclude organic changes and possesses no absolute value; indeed, in certain conditions, as in hypersecretion of the choroid plexus as the result of toxic stimulation and in arteriosclerosis involving the meningeal vessels with the production of hypertension and increased production of fluid, there may be an actual decrease in protein.

The older methods of protein determination were usually more or less intricate quantitative chemical tests; owing principally to the work of Nonne and Apelt, whose famous "Phase I Reaction" is well known, simpler qualitative tests have been devised, which are within the scope of work of any physician trained in laboratory methods. In my experience the Nonne-Apelt test is not sufficiently delicate for practical purposes; the Pandy and Noguchi tests are equally as simple and more delicate. More recently Mayerhofer has advocated a measure

of the protein content by the reduction of a decinormal solution of potassium permanganate when boiled in a strongly acid medium, the amount reduced by 1 c.c. of fluid being called the "permanganate reduction index." This amount was usually between 2 and 2.3 c.c. in normal fluid, while in pathologic fluids, and particularly in tuberculous meningitis, larger values were found. In my experience this test has not yielded information of more practical value than that obtained with the simpler protein tests.

Dextrose.—As previously stated, normal cerebrospinal fluid when boiled with Fehling's solution will reduce the copper. The reducing substance is now regarded as dextrose. A marked *decrease* in dextrose is found quite commonly in the acute infectious meningitides of meningococcic and to some extent in the infections of pneumococcic, streptococcic, and tuberculous origin. In meningococcic meningitis, or the well-known epidemic cerebrospinal meningitis, the fluid may fail altogether to reduce Fehling's solution, and this simple test has been adopted by many physicians in the routine examination of cerebrospinal fluid. In acute meningeal congestion or the so-called "serous meningitis" the amount of dextrose is usually unchanged. In chronic meningitis and in tabes dorsalis, paresis, and cerebrospinal syphilis a decrease in dextrose is not unusual; Hopkins has found low values in syphilis, the decrease being frequently so marked as to give values ranking next to meningitis.

The cause of this reduction of dextrose in the cerebrospinal fluid in disease has been variously explained. In acute suppurative meningitis it is supposed that the bacteria consume the sugar as a food substance, and as recovery takes place with coincident increase in the numbers of bacteria dextrose gradually reappears in the fluid. Mestrezat also explains the decrease on the basis that the large numbers of cellular products of inflammation, red and white corpuscles, absorb a portion of the dextrose. The subject requires experimental investigation.

The most marked increase of dextrose is found in diabetes mellitus; high values have also been found in pneumonia, typhoid fever, epilepsy, and tumors when there is a coincident congestion

of the meninges with the passage of dextrose from the blood to the cerebrospinal fluid. In acute meningitis there is probably the same tendency to increase, which is counterbalanced by active consumption of the dextrose by the invading bacteria.

A simple routine test for dextrose consists in mixing equal parts of Fehling's copper and alkaline solutions and diluting with 9 parts of water; after heating a portion to boiling, an equal part of cerebrospinal fluid is added and the mixture reheated to the boiling-point. This simple test is very serviceable in the study of the fluids in acute meningitis when no reduction at all takes place, but otherwise a more accurate quantitative method is necessary; Bang's micromethod is endorsed by Hopkins and others, is relatively simple, and does not require much fluid for analysis.

Chlorids.—In acute inflammation of the cerebral and spinal meninges the chlorid content of the fluid is reduced. Slight reduction (0.7 per cent.) is usually found in cerebral congestion and edema; marked reduction (0.64 to 0.6 per cent.) in acute meningitis. In tuberculous meningitis the chlorids may sink to 0.5 or 0.6 per cent. In subacute and chronic meningitis the reduction is much less. An estimation of the chlorids, therefore, possesses value in differentiating between infections accompanied by acute meningeal congestion only and true suppurative meningitis and particularly tuberculous meningitis; also in differentiating between myelitis and meningomyelitis, encephalitis, and meningo-encephalitis. An increase of sodium chlorid is frequently found in renal insufficiency.

THE DIAGNOSTIC VALUE OF CYTOLOGIC EXAMINATIONS OF THE CEREBROSPINAL FLUID

Normally the cerebrospinal fluid contains a very few cells, the number varying from 0 to 8 per cubic millimeter of undiluted fluid. From 10 to 12 cells constitute a probable increase, while 15 cells or more constitute a definite increase, generally designated by the term "pleocytosis."

The few cells to be found in normal fluid resemble small lymphocytes of the peripheral blood and tissues and are prob-

ably swept into the fluid during its production; very occasionally an endothelial cell from the lining pavement of the meninges may be found.

Total Number of Cells.—In many diseases of the cerebrospinal system an increase of cells is found in the cerebrospinal fluid; the largest numbers occur in the different forms of infective meningitides, meningococcic, pneumococcic, tuberculous, and poliomyelitic, the total number bearing a more or less direct relationship to the severity of the infection. A slight increase in the total number of cells is usual in organic diseases of the cerebrospinal system, particularly those of syphilitic origin, as paresis, tabes dorsalis, and early gumma; also in herpes zoster, abscess, and tumors of the brain and cord. In counting the total number of cells, I have found the Fuchs-Rosenthal chamber very satisfactory, and particularly when relatively few cells are present.

Kinds of Cells.—During disease a variety of cells may be found, and the subject has been extensively studied during recent years. In the acute infectious meningitides involving the surfaces of the meninges, cord, and brain, as those due to the meningococcus, pneumococcus, streptococcus, and influenza bacillus, the ordinary polymorphonuclear leukocyte predominates, as would be expected. During the earliest stages of acute anterior poliomyelitis and tuberculous meningitis this cell may also predominate, to be quickly followed by a preponderance of small lymphocytes. In chronic diseases of the cerebrospinal system a variety of cells may be found, of which the small lymphocyte and plasma cell from the blood and tissues and endothelial cells from the meninges predominate. A large number of different cells have been described, but it appears to me that many of the bizarre forms to be found are the result of degenerative changes and alterations in the above-mentioned cells due to the method of preparing the slides.

With the exception of the lining endothelial cells of the meninges and plexuses and newly formed tumor cells, the cells found in cerebrospinal fluid in disease are derived from the surrounding blood-vessels and tissues by a process of diapedesis during the changes consequent to inflammation and the increased

transudation of serum from the congested blood-vessels. Here I cannot discuss the various views held regarding the source of the different varieties of lymphocytes, plasma cells, fibroblasts, and other cells; they are present in the tissues of the cerebrospinal system in obeyance to the same rules that govern their development and presence in pathologic conditions in other parts of the body as the result of different agencies, of which may be mentioned positive chemotaxis, mechanical washing into the fluid by the tissue juices, exudation of serum from blood-vessels, and exfoliation.

Cytodiagnosis.—This phrase refers to the diagnostic value of an examination of the cells; generally it refers to a study of the kind or kinds of cells to be found, but may also be employed to include the diagnostic value of the total number of cells present.

A great deal of work has been done and much has been written on the subject in efforts to discover typical and diagnostic changes in the cells in different diseases of the cerebrospinal system. As far as I am aware, there is no typical or diagnostic cell for any single disease of these tissues, unless we except the tumor cell, which on rare occasions has been recognized in the fluid during life and before operation and used as the basis for an opinion and diagnosis. Both the total number of cells and kind of cells in the cerebrospinal fluid are governed by the same laws as are in force in other parts of the body; in acute diseases of infectious origin the polymorphonuclear leukocyte predominates; in chronic infections the small lymphocyte. In the specific infections, as tuberculosis, syphilis, and poliomyelitis, the small lymphocyte is likely to predominate after the very earliest stage, just as it does in the tissue reactions of these infections.

As previously stated, the number of cells present depends upon the severity of the disease and the tissues involved; that is, whether the surfaces of the meninges are principally involved, as in meningococcic meningitis, when the greatest increase occurs, or, the deeper or interstitial tissues of the meninges, as in poliomyelitis, tuberculosis, and syphilis, when the increase is less; or, the tissues of the cord and brain are primarily involved, as in tabes dorsalis and a large variety of degenerative lesions, when

the changes in the cytology of the fluid are likely to be slight or nil. Probably the total cell-count alone has its greatest value in aiding the diagnosis of acute anterior poliomyelitis, in which disease there occurs an early but relatively slight increase in the cells of the small lymphocyte variety. The same is true of tuberculous meningitis, but the symptoms are usually different, and the fluid is more likely to show a greater increase of protein, and prolonged search frequently reveals the presence of the tubercle bacillus.

It is necessary, therefore, for the physician to bear in mind the pathology of the disease under consideration in interpreting the results of total and differential cell counts; under these conditions the total count may be an index of regression or progression of the disease and of value as an index in treatment. Total and differential cell counts possess, therefore, a distinct value in the examination of the cerebrospinal fluid when considered with the results of the examination of the fluid and the clinical aspects of the patient.

THE DIAGNOSTIC VALUE OF BACTERIOLOGIC EXAMINATIONS OF THE CEREBROSPINAL FLUID

Common experience has shown that early and specific diagnosis of a disease is best accomplished, or, indeed, only possible, when the specific cause of the disease can be found without undue delay. For this reason a bacteriologic examination of the cerebrospinal fluid is of great importance, and especially in the diagnosis of the acute meningitides due to the meningococcus, pneumococcus, streptococcus, Bacillus tuberculosis, and B. influenzæ.

The normal cerebrospinal fluid is a poor culture-medium, but in inflammatory conditions the increase in protein and dextrose improves the cultural properties.

In many instances the bacteriologic diagnosis may be made by microscopic examination of stained smears of the sediment secured by centrifuging a portion of the fluid. This enables a quick and usually accurate diagnosis, but it is good practice to verify these findings by cultural methods. The fluid should be

collected under strict aseptic conditions, and in preparing cultures a rich medium, as blood-agar or Löffler's blood-serum, should be employed. Furthermore, unless smears show an abundance of micro-organisms, it is well to culture a large amount of fluid (at least 1 c.c.) or, better still, to centrifuge the fluid with aseptic precautions and culture the sediment. As many of the micro-organisms are apparently already dead or devitalized when the fluid is secured, it is well to prepare the cultures as soon as possible after withdrawal of the fluid.

In tuberculous meningitis the bacilli are usually to be demonstrated by centrifuging the fresh fluid at high speed for one-half hour, and preparing smears of the sediment, or by patiently teasing apart on a slide a portion of the fibrin coagulum which forms a few hours after the fluid has been collected. In either case the smears are stained by the usual technic for acid-fast bacilli, and prolonged search is generally necessary before the bacilli are found. Great care must be exercised against regarding acid-fast artefacts as tubercle bacilli.

Treponema pallida have been found in the cerebrospinal fluid by Hofman, von Dohio, Noguchi, Nichols and Hough, Wile, and others by direct microscopic examination, and particularly by inoculation of the fluid into the testicles of rabbits. The trypanosome of sleeping sickness has been found in the fluid by Castellani, Bruce, and others; Cysticercus cellulosa has been found by Hartman and actinomyces by Sicard, but these findings are unusual, and bacteriologic studies are generally confined to the diagnosis of the various forms of acute meningitis mentioned above.

Recently a great deal of attention has been devoted to the bacteriology of acute anterior poliomyelitis. The fundamental experiments of Flexner and Lewis, Landsteiner and Levaditi, and others have proved that the disease is of microbic origin, and the globoid bodies cultivated by Flexner and Noguchi from tissues of the central nervous system of fatal cases have the strongest claim as being the etiologic agent of the disease, but none of the methods employed for demonstrating the presence of the virus or globoid bodies are adapted for practical diagnostic purposes.

While experimental evidence teaches that one portal of entry of the virus is the mucous membrane of the upper respiratory tract, and that the secretions may harbor the microparasite, a demonstration of the presence of the virus is only possible by monkey inoculation, requiring many days or weeks of time, which places this test beyond the pale and scope of practical diagnosis. While the recent reports of Mathers, Rosenow, Nuzum, and Herzog indicated that the etiologic agent of acute poliomyelitis was an easily cultivatable diplococcus or streptococcus, and that, indeed, the diagnosis of a case may be made by culturing the cerebrospinal fluid with almost the same ease and sureness with which typhoid fever may be detected in the early stage by blood-culture, it is highly probable that their reports served only to renew interest in some of the oldest bacteriologic findings in the disease, and have failed to establish these cocci as the cause of acute poliomyelitis. Drs. Brown, Freese, and I have found these diplococci and streptococci not only in the cerebrospinal fluid, brain, and cord but also in various internal organs of fatal cases of poliomyelitis, but all of our inoculation tests have failed to show that these micro-organisms were capable of producing the disease in rabbits or monkeys. On the other hand, these cocci have occasionally produced meningitis, arthritis, pleuritis, pericarditis, and other inflammatory lesions in the experimental animals, indicating that they may possess some degree of virulence, and are probably not to be classed as strictly saprophytic; furthermore, the complement-fixation tests conducted by Dr. Freese and I have shown that antibodies for these cocci may occasionally be found in the body fluids of persons suffering with acute poliomyelitis, and Cohen and Heist have recently shown that the sera of convalescents and of animals immunized with these diplococci contained an increased amount of what appeared to be a specific opsonin, indicating some relationship between these micrococci and poliomyelitis analogous to the relationship of streptococci to scarlet fever. In the experiments of Bull the lesions produced in experimental animals by streptococci cultivated from the tonsils of persons suffering with acute poliomyelitis were entirely similar to those produced

by streptococci from other sources, and it would appear as definitely established that these micrococci bear no direct relationship to the etiology of epidemic poliomyelitis. While the true nature of the globoid bodies is as yet unknown, and their relationship to poliomyelitis requires more wide-spread confirmation before being finally accepted as the cause of this disease, it is at least evident that we do not possess the one and only early and specific means of diagnosing the disease, namely, the ready demonstration of the specific microparasite.

THE DIAGNOSTIC VALUE OF IMMUNOLOGIC EXAMINATIONS OF THE CEREBROSPINAL FLUID

As the cerebrospinal fluid is normally derived from two principal sources—namely, as a secretion of the choroid plexus and possibly as a more or less selective filtration of fluid from the vessels of the meninges—it is practically devoid of those natural immunity principles so commonly found in the blood-serum as complements, bacteriolysins, diphtheria antitoxin, and various hemolysins. During diseases without involvement of the meninges, when antibodies reach a high degree of concentration in the blood, traces of them may be found in the cerebrospinal fluid, like agglutinin for Bacillus typhosus during the height of typhoid fever. Likewise in syphilis, and particularly during the secondary stage, the cerebrospinal fluid may react positively without the patient showing any clinical evidences of involvement of the cerebrospinal tissues. It is possible that the Wassermann antibody reaching a high concentration in the blood is passively transferred to the spinal fluid in a similar manner. With involvement of the meninges, as acute meningeal congestion or "serous meninges" (meningismus), there occurs a greater transudation of serum or a hypersecretion of the fluid with a corresponding decrease of selective filtration, with the result that antibodies are more readily transferred from the blood to the cerebrospinal fluid. In suppurative meningitis the disintegration of leukocytes also furnishes various substances of a bacteriolytic nature and complements may now be present. The Weil-Kafka hemolysin reaction is based upon these prin-

ciples; natural antisheep hemolysin is present in the blood-serum of over 90 per cent. of individuals, but is absent from the normal cerebrospinal fluid, whereas in meningitis with consequent disturbances of the production of the fluid, this hemolysin alone or in conjunction with hemolytic complement may find their way into the cerebrospinal fluid. This reaction demonstrates, therefore, disturbance of the mechanism concerned in the production of cerebrospinal fluid as occurs in a high percentage of cases of acute meningitis, and also to some extent in the more chronic forms due to syphilitic infection.

While various biochemic or immunologic reactions have been described, as the precipitin reactions of Porges and Meier, Herman and Perutz, and the more recent "gel" test of McDonogh, in the diagnosis of syphilis, only two tests are of wide-spread and proved value, namely, the Wassermann and Lange colloidal gold reactions. Both are reactions of syphilitic involvement of the cerebrospinal system. As we have no immunologic reactions for benign and malignant tumors (gumma excepted), as the acute meningitides are usually to be recognized on the basis of bacteriologic examination, and the microbic cause of many other chronic diseases, as the psychoses, scleroses, syringomyelia, etc., are unknown, if they exist at all, immunologic investigation has naturally centered upon syphilis as a result of the frequency with which pallidum involves the nervous tissues, and the intense research interest shown in this disease during the past fourteen years.

Specificity of the Wassermann Reaction.—The Wassermann reaction is not biologically specific, but practically it possesses a high degree of specificity due to the fact that the peculiar lipoidophilic reagin or Wassermann antibody is found in so few other diseases. This reaction, however, has been so universally used and misused that there are very few diseases in which some investigator has not reported positive results. At present it is known that positive Wassermann reactions may occur in a few diseases other than syphilis, but not to the extent that earlier investigators would have us believe. In most of the diseases yielding positive reactions, such as frambesia (yaws) and leprosy

of the tuberous type, the clinical symptoms are so marked that they may readily be differentiated from syphilis, so that in those parts of the world where frambesia does not occur and leprosy is rare, the Wassermann reaction with either serum or cerebrospinal fluid is of unequalled and incalculable diagnostic value. Of great importance, however, is a thorough understanding of the underlying principles of the reaction and its technic, as the majority of positive reactions reported as occurring in the large group of various diseases can be ascribed to faulty technic.

The technic, while comparatively simple, has many sources of error, most of which are controllable, but require a thorough understanding in order that an intelligent and reliable complement-fixation reaction may be secured. Those attempting this reaction should have accurate knowledge of the preparation and standardization of the antigen or extract and know a good from a poor one; I believe the antigen constitutes one of the most important elements of the reaction and explains the discrepancies among results from different laboratories more than any other single factor. Likewise, the worker should have intimate knowledge of the sources of error dependent upon the serum alone and the various components of the hemolytic system, as complement, hemolysin, and corpuscles; the importance of at least chemically clean glassware and other modifying factors should be borne in mind, since they influence the results.

Diagnostic Value of the Wassermann Reaction in Syphilis of the Cerebrospinal System.—The statement is frequently made that a diagnosis of syphilis should not be based upon the results of laboratory examinations. In not a small group of cases, however, the diagnosis cannot be made otherwise. In the latent cases of long standing and in the tertiary stages of syphilis the Wassermann reaction may be the only available basis upon which to establish a diagnosis. As a diagnostic measure every safeguard must be placed about the test to avoid non-specific reactions. While it is true that great harm may result from a false positive diagnosis due to faulty technic, yet it must be admitted that the Wassermann reaction is not too

delicate, and that we are liable to err on the side of securing false negative reactions. Every effort should be made to render the test as delicate as possible with reliability and specificity; in my opinion this is best secured by the closest attention to the kind and dose of the antigen, and, second, to quantitative factors in the hemolytic system.

Persons with syphilitic involvement of the cerebrospinal tissues may yield positive reactions with both blood and cerebrospinal fluid, or, what is very important for the surgeon to bear in mind, may react positively with the fluid and negatively with the serum, a matter difficult to explain, and believed to be due to the confining of the reacting substances in the subarachnoid space. Occasionally the reaction may be positive with the serum only, but it is important to remember that before a diagnosis of syphilitic disease of the cerebrospinal tissues can be excluded on the basis of the Wassermann test both serum and fluid should be examined.

Normal cerebrospinal fluid does not give a positive Wassermann reaction; the fluids of persons suffering with frambesia (yaws) or leprosy may yield a positive reaction in the absence of syphilis. In paresis and taboparesis the blood Wassermann is positive in 90 to 100 per cent. of cases; the spinal fluid Wassermann is positive in at least 85 per cent. of cases, using 0.2 c.c. of fluid after the original method, and in about 72 to 100 per cent. of cases, using larger doses of fluid (0.8 c.c. or more) after Hauptmann's method. In tabes dorsalis the blood-serum reacts positively in from 96 to 100 per cent. of cases; the spinal fluid reacts positively in about 60 per cent. unless large amounts of fluid be used (0.8 c.c. or more), when positive reactions are observed in about 87 per cent. In cerebrospinal syphilis the blood-serum, and particularly the fluid, will give a positive reaction less frequently than in paresis. In untreated congenital syphilis of children one year or over in age the blood Wassermann reaction is positive in from 97 to 100 per cent. of cases. As the clinical manifestations may vary and be ill-defined, the serum reaction possesses considerable diagnostic value. Likewise, in congenital mental deficiency and epilepsy the Wassermann reaction shows

that syphilis plays a part in the etiology of a small proportion of cases.

In the primary stage of syphilis the cerebrospinal fluid reacts negatively; in the secondary stage, however, the fluids of a number of cases showing no symptoms referable to the central nervous system have been found by Craig and Collins and Wile to react positively. This indicates that these tissues may be involved comparatively early in syphilis, but a positive Wassermann alone cannot be interpreted as positively indicating involvement of the nervous tissues, as it appears possible for the Wassermann antibody or reagin to gain access to the fluid from the blood-serum. In gumma of the brain or spinal cord the Wassermann reaction possesses a very distinct value in diagnosis.

Provocatory Stimulation.—Occasionally persons are encountered presenting indefinite symptoms of involvement of the tissues of the central nervous system and a negative or doubtfully positive Wassermann reaction, while syphilis is known to have been contracted or is strongly suspected. In these the intravenous administration of 0.4 gm. of salvarsan, followed two or three days later by a second Wassermann reaction, may result in securing positive and conclusive results. This is known as provocatory stimulation, and is due probably to the liberation of endotoxins from destroyed treponemata or to their stimulation by a dose of drug that did not suffice to kill them, an analogy to the clinical Herxheimer reaction.

The Wassermann Reaction and Its Relation to Treatment.—Citron originally observed that during the mercurial treatment of syphilis the Wassermann reaction gradually became weaker and finally disappeared. His observations, which have since been confirmed, showed that the Wassermann reaction may be taken as an index and guide to treatment. It should be the object of treatment not only to dissipate the external and obvious lesions of the disease, but to produce a condition of the blood and cerebrospinal fluid in which the Wassermann reaction is permanently negative.

In my experience it is often an exceedingly difficult matter to influence the blood or fluid Wassermann reaction of well-

developed cases of syphilis of the central nervous system, especially in paresis and taboparesis, by vigorous treatment with salvarsan or mercury or a combination of these. Objective and subjective symptoms may be relieved or entirely disappear, or the lesions may at least be prevented for a time from further development, but complete cure on the basis of clinical aspects and negative Wassermann reactions is decidedly uncommon. Despite most vigorous treatment with intravenous and intraspinal injections of salvarsan, persistently positive Wassermann reactions are observed with the spinal fluid. When this condition of "Wassermann-fast" reaction occurs with the fluid of a tabetic, Kaplan suspects the development of paresis. The sum total of the experience of investigators from all parts of the world would indicate that a persistently positive reaction means the presence of living Treponema pallida somewhere in the body, and that treatment should be continued until the blood and cerebrospinal fluid reacts negatively. Among cases showing in the spinal fluid (1) a pleocytosis, (2) increased protein content, and (3) a positive Wassermann reaction, the pleocytosis is generally first reduced by treatment, then the second, and lastly the Wassermann reaction. The latter, therefore, constitutes the most delicate index of treatment. It has been abundantly proved, however, that a single negative reaction with the blood or fluid is not sufficient or definite evidence that a cure has been effected, for the reaction may recur after treatment is discontinued and be followed by clinical evidences of the disease. It is necessary, therefore, that the reactions remain persistently negative over two years before a cure can be declared.

Lange's Colloidal Gold Reaction.—The main drawback to the employment of this test is the difficulty of preparing the reagent in a suitable and stable form. I have been most successful with the technic described by Miller, Brush, Hammers, and Felton, but, despite rigid adherence to the principles and instructions in every detail, I have a high percentage of failures in obtaining a fluid answering the best requirements. The technic of the test itself is extremely simple and the readings usually not difficult, particularly with the cerebrospinal fluid of a paretic.

The nature of the reaction is not understood. Lange apparently regards the precipitation of colloidal gold due to the presence of a protein, but this is doubtful, as it has been shown that globulins and peptones may actually protect colloidal gold against precipitation, and while partial precipitation occurs with the cerebrospinal fluids of acute meningitis of meningococcus, tuberculous, and poliomyelitic origin, and syphilis other than paresis, the typical reaction is observed in paresis. It would appear, therefore, that exact quantitative proportions of a protein were necessary for the typical reaction, which, if true, occurs in paresis, or that some undiscovered principle or substance is concerned in the reaction.

The practical value of the test is principally confined to the diagnosis of paresis. Even before the distinctive symptoms and signs of this malady are present the colloidal gold test may yield a well-marked paretic reaction, characterized by complete decolorization of the first three or four tubes, and thus place the physician and relatives of the patient on guard against the moral delinquencies accompanying this disease.

Types of reactions are also observed in other syphilitic diseases of the cerebrospinal tissues, as in tabes dorsalis and cerebrospinal sypilis, also in various forms of meningitis, but the most definite value of the reaction, as a practical diagnostic procedure of considerable reliability, is in paresis.

CONCLUSIONS

It is readily understood that with the majority of diseases of the cerebrospinal system, accompanied by demonstrable changes in the cerebrospinal fluid, the diagnostic value of spinal puncture and an examination of the fluid is best appreciated with a complete analysis of the fluid, and by the physician who understands the underlying principles governing the pathologic changes which may occur. Aside from finding the specific micro-organisms of a disease in the cerebrospinal fluid, there is no other single specific change except possibly the Wassermann reaction, which, when positive, indicates that the patient is infected with syphilis and that the nervous tissues *may* be involved, and

the colloidal gold reaction, which, when yielding a typical paretic curve, indicates paresis. Even in these latter conditions other data, as a protein determination and total cell count, are valuable in aiding the diagnosis, as exemplified in the famous "four reactions of Nonne," namely, a total cell count, protein determination, and Wassermann reaction with cerebrospinal fluid and blood-serum.

With the cloudy or purulent fluid of acute meningitis in which the micro-organisms are found by smear or culture nothing more is necessary for diagnosis, although cell counts and protein determinations furnish data indicating the severity of the infection, and serve as guides, indicating regression or progression of the disease under treatment; in practically all other conditions more complete studies according to the following outline are necessary before the full value of a cerebrospinal fluid examination is to be appreciated:

Pressure as taken with the Landon manometer and in a uniform manner, preferably, with the patient lying on the left side.

Physical appearance of the fluid.

Total cell counts made with fresh warm fluid and, preferably, with the Fuchs-Rosenthal chamber.

Differential cell counts made with direct smears of the sediment secured by thorough centrifugalization or by the Alzheimer method.

Protein determination, employing the Noguchi, Pandy, or Kaplan tests.

Sugar determinations, employing the simple and rather crude Fehling's reagent or the more accurate micro-method of Bang.

The Wassermann reaction, employing graded amounts of fluid up to and including a dose of at least 1.5 c.c.

The Lange colloidal gold-test, employing an acceptable reagent.

Bacteriologic examinations if the presence of bacteria are suspected; by direct examination of stained smears of sediment or cultures of the sediment on appropriate culture-media. Animal inoculation tests may be employed for the detection of tubercle bacilli and Treponema pallida.

CLINIC OF DR. JOHN H. MUSSER, JR.

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A CASE OF AURICULAR FIBRILLATION OF LONG DURATION

IN considering bodily disorders which have been recognized but a short time it is obvious that their duration cannot be accurately foretold. This statement applies particularly to some of the disorders of the cardiac rhythm which have been studied by means of the electrocardiograph, an instrument which has been elaborated within the past few years. Previous to the practical application of this machine in the study of irregularities of the heart but little was known of their cause or their mechanism. They were recognized clinically, but here the knowledge about them stopped; for example, the absolutely irregular pulse had been known for years, but it was not until Dr. Lewis[1] studied cases with absolute irregularity by means of the string galvanometer that he was able to determine that the irregularity was due to fibrillation of the auricle. Previous to this the possibility had been suggested by Cushny,[2] Mackenzie,[3] and Wenckebach,[4] but it was not until 1909 that Lewis firmly established the clinical entity of the disorder. It is thus seen that it has been only a comparatively short time that such cases could be accurately studied. Shortly after the work of Lewis appeared the disorder was, as a rule, thought to be of extremely short duration and very often a terminal event. As the years have gone by it is plain that this conception has been materially altered. Under certain conditions it is now becoming recognized that auricular fibrillation may persist for years. A review of some of the recent articles which have to do with auricular

fibrillation shows that the previous conception of the duration of the disorder is changing, and that the onset of the condition is now realized to be an unfavorable but not necessarily a prognostic omen of severe import. Lewis,[5] in discussing the prognosis of auricular fibrillation, says that "it loads an already defective muscle with an extra and appreciable burden. In most cases it heralds cardiac failure, temporary or terminal, so that few patients survive its onset for more than ten years." Osler[6] writes that "the condition may last for many years when once established. . . . An unduly grave view must not, therefore, be taken unless there be marked evidence of cardiac failure." Mackenzie,[7] in a most comprehensive summary of the prognosis of the condition, says that "there are many individuals with fibrillation who lead useful and energetic lives, and whose capacity for work is little if at all impaired by the new rhythm. In such the prognosis is distinctly good." Two other expressions of opinion in current literature may also be mentioned. Herrick[8] calls attention to the fact that, although "prognosis has generally been held to be bad, the condition may last for years, even ten or more." Pardee,[9] in an article on the prognosis of auricular fibrillation, emphasizes the necessity of continuous treatment in these cases, and shows that, with proper medication, the patients suffering with the disorder may survive for years, and concludes that "the irregularity *per se* adds little or nothing to the gravity of the prognosis of the individual."

The case of auricular fibrillation that I wish to report is of interest because of the presumably prolonged duration of fibrillation—some twenty years. The proof of this statement may be questioned, but I will attempt to show in the discussion of the case that my facts are sufficiently conclusive to warrant the statement that the patient lived for at least twenty years with the auricles continuously fibrillating.

Case History.—Mrs. M. S., Hospital No. 60,456, dressmaker, age fifty-eight.

Chief Complaint.—Cough, general malaise.

Present Illness.—Since October 26th the patient has had a heavy cold on her lungs. It began with a chill and severe head-

ache. The cough is worse at night; not very productive except in the mornings. Anorexia. Bowels are constipated. There is a slight sore throat. The patient has a severe pain and marked tenderness in the right flank which has been present since last July, but this has been intensified by her lung condition.

Family History.—Father died of ulcer of stomach; mother, of intestinal obstruction. One sister has rheumatism and kidney trouble.

Personal History.—Usual diseases of childhood—diphtheria, scarlatina, typhoid fever—twenty years ago. No rheumatic fever. Has had sore throat and bronchial trouble. She says that she has heart trouble. She often gets short of breath, but has never had edema except an occasional slight swelling of the ankles in the evening. About twenty years ago she had her ovaries removed. Two years later she took a six weeks' rest-cure for a run-down condition. Ten years ago she was in the hospital again for la grippe and heart trouble. Five years ago had a painful condition of feet; was in the hospital for three months. Last July the patient was again in the surgical service of this hospital for a painful condition in her right flank. She states that her heart has long been affected. She has not been particularly well since her last discharge.

Menstrual History.—Menses began at sixteen. Were always regular, extremely painful. Persisted six days. Last period just before removal of ovaries twenty years ago.

Social History.—Was married; self-supporting dressmaker.

Physical Examination.—Patient is a middle-aged woman, underdeveloped and undernourished. Lies quietly in bed and apparently has no pain, but coughs quite a good deal.

Eyes.—Pupils equal and regular, react readily to light and accommodation. No nystagmus, von Grafe, nor Stellwag sign. There is a slight ptosis of the upper left lid. Sclera clear, conjunctiva pale.

Ears.—No tenderness nor discharge.

Throat.—Slightly congested, tonsils not enlarged but cryptic, and contain some cheesy material. Tongue clean. Teeth in good condition. Mucous membrane of mouth pale.

Neck.—No adenopathy, no abdominal pulsations. There is, however, a retraction of the tissues of the neck just above the clavicle during the systole of the heart.

Thorax.—Rather poorly developed, being of the narrow shaped type. There is greater expansion on the left than on the right side.

Lungs.—The percussion-note is slightly higher pitched on the right side anteriorly than it is on the corresponding side. This is also true posteriorly in the upper lobe. On the right side anteriorly and posteriorly the expiration is prolonged somewhat in the upper lobe. On the left side anteriorly the expiration is jerky and seems to be prolonged. The spoken voice sounds are slightly better heard on the right side in the upper lobe than they are on the opposite side. There is no change in the whispered voice sounds. There are a few crepitant and subcrepitant râles heard throughout both lungs anteriorly and posteriorly.

Heart.—Very slight impulse seen and felt over the precordium which is limited to the apex region. No shock or thrill palpable. Apex-beat not diffuse and best palpable in the fifth space, midclavicular line. Area of cardiac dulness: upper border, second rib, to right border of sternum, to left border, 12.5 cm. to left of midsternum. Sounds quite rapid and absolutely irregular, a beat missing from the wrist every ten to fifteen beats of the heart; muscular and valvular tone fairly good. No murmurs heard.

Pulse.—Irregular, at times appearing to be dicrotic. Some of the cardiac beats do not come through to the radial pulse. The volume is poor, but the tension is good.

Abdomen.—On level with the chest, tympanitic throughout. Slight tenderness over the whole abdomen, especially on the right side over the kidney region. There is no muscular rigidity. The liver and spleen are not palpable. The right kidney is doubtfully palpable; the left cannot be felt.

Extremities.—Negative.

Reflexes.—Normal. Slight tremor of hand.

Skin.—Moist; no rashes.

Urine.—Sp. gr. 1018; reaction acid; sediment flocculent; albumin very faint trace; no sugar; few hyaline and granular casts; epithelial cells and W. B. C. phenolphthalein elimination: first hour, 20 per cent.; second hour, 25 per cent.

Blood.—Red cells, 4,840,000; leukocytes, 8,400; hemoglobin, 80 per cent.

Sputum.—No predominating organism; few Gram-negative cocci; staphylococci, diplococci, streptococci. Very few encapsulated organisms. No tubercle bacilli found.

November 3: Heart borders as above except that right border is approximately 3 cm. to right of sternum. The first sound at

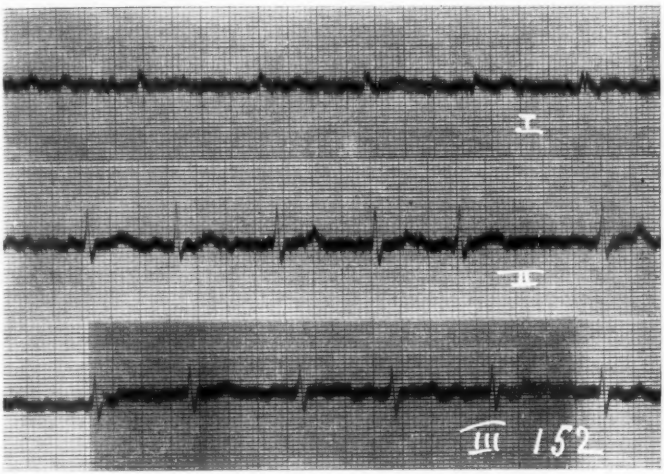

Fig. 33.—Electrocardiogram of M. S. taken November 3d, showing auricular fibrillation with slow ventricular rate.

apex is loud and sounds are absolutely irregular, and before an occasional slow beat there can be heard a distinct presystolic murmur which is not transmitted. The second aortic sound is slightly accentuated. No tubercle bacilli in sputum.

November 4: Temperature has been down now for the past four or five days; coughs much less, but there are a few râles heard in both lungs. Heart still irregular. Roentgenogram of heart shows marked enlargement to the right.

November 5: There is a suggestion of a thrill at the apex. Posteriorly over the left lung, beginning at the tenth rib, the note is slightly higher pitched than on the corresponding side, but there is no change in the fremitus nor breath sounds. There are a few sonorous râles heard anteriorly over the left lung below the fifth rib, but otherwise the lungs are negative. Sputum negative for tubercle bacilli on last two examinations. Wassermann reaction negative.

November 10: Patient developed a slight facial palsy last night, the paralysis being on the right side. It involves the

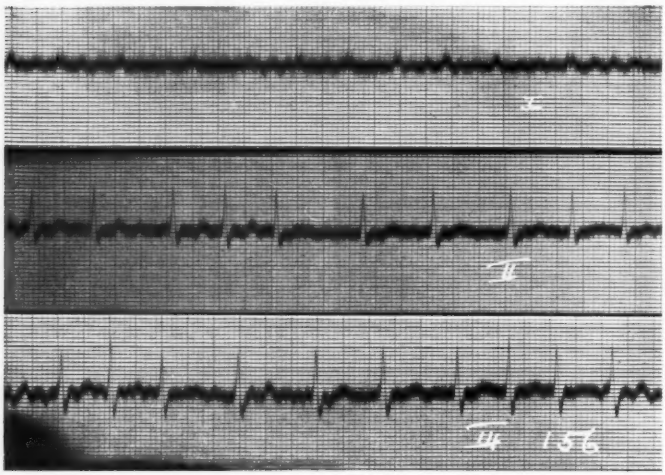

Fig. 34.—Electrocardiogram of M. S. taken November 10th, again showing auricular fibrillation with rather slow ventricular rate.

eyelid, face, tongue, and lips. The patient has difficulty in articulating properly. Examination shows the ears, nose, and throat to be practically negative. Eye-grounds negative. Patient appears to be much weaker and moans a great deal, but says she has no pain. Lungs clear.

November 11: The facial palsy is just about the same. Patient also has trouble in articulating, being able to say only a few words. Today patient has rather severe pain in left flank and epigas-

trium. There is tenderness, on the left side particularly. There is some rigidity in the left abdominal muscles. Leukocytes are up to 21,400 and the urine shows red blood-cells. Patient seen by surgeon, who thinks that there is probably a renal stone or an infection of the pelvis of the kidney.

Urine.—Sp. gr. 1032; reaction acid; sediment flocculent; cloud of albumin; no sugar; few hyaline and granular casts. A few epithelial cells and W. B. C. Occasional R. B. C.

November 13: Patient continues to complain of pain about the left kidney and radiating down the flank and anteriorly. Temperature and leukocytes are up. Facial paralysis no better and the ability to speak has not improved, patient being able to say only "yes" and "no." The lungs are clear except for an occasional râle heard posteriorly. Pulse slightly weaker than it has been.

November 16: Temperature has been normal now for the past three days and patient has been free of pain most of the time. However, she has a slight cough. Urine still has some red blood-cells. Facial palsy just the same; also the speech. Lungs clear. No change in the cardiac condition.

November 19: Patient seems to be getting worse. The temperature is very irregular, most of the time being subnormal. Patient seems more dull and apathetic. Facial palsy no better. While patient is unable to say even the words "yes" and "no," she apparently understands when spoken to and easily recognizes objects. Cardiac condition about the same.

November 22: Cystoscopic examination showed the bladder to be normal. The left ureter could be catheterized with a small catheter, and the catheter could be passed into the pelvis of the kidney. The right ureter could not be catheterized, probably on account of the end of the catheter being caught in the mucous membrane, but the ureter was patulous, as urine could be seen coming from it.

November 23: Patient was apparently the same until last night, when she had a good deal of pain and became pulseless at the wrist. The right side of the body twitched as though she were having a convulsion, and the left side of the body became

paralyzed. When seen this morning the patient had a set, fixed expression. The left side of the body was in a state of flaccid palsy, while the right side was more or less rigid and could be moved. The left leg was cold and blue. The pulse was still irregular, full, and bounding. Patient was unable to speak at all and apparently unable to understand.

November 25: Patient is still paralyzed on the left side. The pulse is very weak, rather rapid and irregular. There are a few râles heard at the bases of the lungs. The left leg is still cold and blue.

November 27: Patient is steadily getting worse. The bases of the lungs are congested and the pulse very weak. No improvement in leg. Patient died without improvement. Death due directly to heart failure.

Diagnosis.—Myocardial insufficiency. Mitral stenosis with auricular fibrillation. Hemiplegia.

Autopsy 286 (abstract, etc.), Nov. 29, 1916:

Anatomic diagnosis: Mitral stenosis, passive congestion of the lungs (hypostatic), chronic interstitial nephritis, old renal infarcts.

Note on pericardium and heart: The pericardial sac contained 75 c.c. of clear fluid. The lining membrane was smooth and glistening.

The heart weighed 250 grams. The auricles were relatively large. The ventricles were of normal or even less than normal size. The wall of the left ventricle was relatively thick. The papillary muscles on the left side of the heart were short and thick. After stretching out the auricles the left was found to measure 10 cm. and the right 8 cm. in length and 6 cm. and 4 cm. in width respectively. (These measurements are not intended to represent the dimensions in a normal position.) The mitral valve curtains were thickened and leathery, and were united at their borders, forming a funnel-like projection, with an opening at the apex of the cone wide enough to admit the tip of the little finger. In the lower portion of the aorta and surrounding the openings of the coronary arteries were areas of atheroma. There were no other valvular lesions.

Discussion.—From the history of the case it is evident that the patient died as a result of the hemiplegia which was brought on by an embolus from the mitral valve to the brain. Likewise from the history and autopsy it may readily be assumed that the pain in the side and the hematuria was also induced by emboli swept into the kidneys which were mildly infectious, causing the temporary rise in temperature and leukocytosis. At no time while at the hospital was there evidence of cardiac insufficiency, and the patient's death was not a cardiac death.

The evidence that the patient had persistently fibrillating auricles is gained by a study of the old hospital record and from a report of the physician who attended the patient in the intervals between the hospital stays. The first hospital record shows that the patient was admitted to the ward in 1896, at which time the diagnosis was made of "neurasthenia following oöphorectomy." The patient is noted at that time as having an irregular heart with a pulse-rate varying from 52 to 104. One month later she was discharged, and at that time a note was made that the heart action was more regular and there was not such a diversity between the beats. There is nothing in the record to indicate that the patient had marked cardiac disturbance.

In 1907 she was again admitted to the hospital for what was thought to be a surgical condition and was treated in the surgical ward. A readmission occurred in 1910. The notes are most incomplete for this visit, but the diagnosis was made of neuritis, and apparently as a result of the cardiac irregularity; strophanthus was given for two months. The pulse-rate at this time varied irregularly between 50 and 92. On the 16th of July of the present year the patient was again readmitted to the surgical ward on account of hematuria. This cleared up in a short time, but while in the ward the pulse-rate again varied at different times of taking between 56 and 96, but there was no evidence of cardiac decompensation. The last admission record has been given in detail in the above history. A personal communication from the patient's family physician tells me that he had had the patient under observation for some fifteen years, and his father before him for some years. During this time Mrs. S. was never

healthy, but was able to go about her business of dressmaking, a most quiet type of occupation, without any cardiac disturbance. Largely the result of continuously irregular heart action she was kept on digitalis practically uninterruptedly during many years.

From the study of the records and from the physician's statement, I believe the evidence is conclusive that the patient had persistent auricular fibrillation for twenty years.

Summary.—A case of auricular fibrillation of long duration is recorded. Aside from the persistency of the condition, it is interesting to note that at no time did the heart muscle show evidence of an insufficiency. Furthermore, the beneficent influence of digitalis and the marked salutary effect upon the prognosis of auricular fibrillation by prolonged digitalis therapy, as emphasized by Mackenzie, is well illustrated by the course of events in the above history.

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CONTRIBUTION OF DR. T. H. WEISENBURG

NEUROLOGIST TO THE MUNICIPAL HOSPITAL AND THE PHILADELPHIA HOSPITAL

POLIOMYELITIS [1]

A Study of the 1916 Philadelphia Epidemic with a Report of 717 Cases.

THE investigation of the epidemic of infantile paralysis consisted in the study of all the cases which were admitted to the Municipal Hospital for contagious diseases and of some of the families from which they came, an effort being made to find out the presence or absence of the so-called abortive types in the other members of the families in whom actual cases of poliomyelitis occurred. A talking machine was used in recording the cases, while in the study of the abortive types a house-to-house canvass was made. In this study I had the assistance of Drs. Perce DeLong, Wm. J. Essickson, J. H. Turner, M. K. Myers, Grayson McCouch, Samuel S. Woody, Chief Resident Physician of the Municipal Hospital, and the resident physicians, who gave invaluable service. I am especially indebted, however, to Dr. Simon Leopold, who personally examined the record of every poliomyelitis patient, and who also is responsible for the data and comments made on the purely medical aspects of the subject.

The information obtained from a study of the predisposing causes of the epidemic may briefly be summarized in the table on page 394.

[1] This paper is one of a number on the study of the Philadelphia epidemic. Other papers on this subject will appear by Dr. Charles K. Mills, Allen J. Smith, J. A. Kolmer, and others.

I. *Sex.*—There were 388 males and 329 females affected in the 717 cases which were studied. These figures correspond to those of the New York epidemic and to those of most observers who state that males are somewhat more frequently affected than females.

II. *Color.*—There were 699 Caucasian and 18 negroes. These figures, *per se*, do not admit of any interpretation regarding sus-

		Non-fatal						Fatal		
		Spinal	Ascending Landry	Descending Landry	Bulbo-Pontine	Hemiplegic	Meningitic	Abortive	All fatal	Total
I. Sex.	a. male	210	19	1	53	5	6	8	86	388
	b. female	187	16	7	31	8	1	4	78	329
II. Color	a. white	387	35	8	81	10	6	12	162	699
	b. negro	11	0	0	4	0	1	0	2	18
III. Age.	under 6 mths	12	2		3	1	1	1	17	37
	6 to 12 mths	62	9		10				57	138
	1 yr.	94	9	5	23	4	2	2	23	162
	2	91	6	2	21	1	2	3	19	145
	3	51	5		13	1	1	2	14	87
	4	34			5	1	1	1	6	48
	5	20		1	4	1		3	6	35
	6	12			1				3	16
	7	2			2				5	9
	8	1								1
	9	3								3
	10	2								2
	10-15	4			1				4	9
	15-20	2			1				4	7
	20-30	2	3							5
	30-40	1							2	3

Fig. 35.—Sex-color-age summary.

ceptibility. There are too many other factors concerned. It was our impression that the disease was more severe among the negroes, the paralysis usually being very extensive, with a very

slow return of function. In the relatively small number of cases the mortality among the negroes was proportionately not as high as among the whites.

III. *Age.*—456 of the 717 cases studied occurred between the ages of six months and three years. There were 37 cases in children under six months. Many of these infants were breast fed. When it was possible, nursing mothers were brought to the hospital with their children. Of the 49 cases which were breast fed, there were only 7 deaths.

IV. *Previous State of Health.*—There was nothing in the previous medical history which can be considered as having any bearing on the occurrence of acute anterior poliomyelitis. The great majority of the children were robust and apparently in perfect health prior to contracting this disease. This is obviously true of most of the acute infectious diseases, and does not have any special significance.

SYMPTOMATOLOGY

These may be classified as those of onset, the preparalytic symptoms, and those occurring during the course of the disease in the paralytic stage. These symptoms, of course, merge and become continuous as the disease progresses.

The preparalytic symptoms were carefully compiled and statistically studied in 716 true cases of infantile paralysis. All cases when there was any reasonable doubt as to diagnosis were discarded.

The table on page 396 shows the preparalytic symptoms which were recorded and their relative frequency.

I. *Fever.*—The most striking fact in reviewing these charts was the very great similarity in the records, to such an extent that it was often possible to make a differential diagnosis between infantile paralysis and various other diseases—*i. e.*, scurvy, various types of meningitis, marasmus, etc.—by a mere glance at the clinical chart. In other words, the clinical course of the disease runs true to type with remarkable consistency. The fever was moderate—100° to 103° F.; in a relatively few cases, mostly in very young children, it was higher, but rarely

	Spinal non-fatal 394 cases	Spinal, fatal 41 cases	Ascending Landry non-fatal 35 cases	Ascending Landry fatal 84 cases	Descending Landr non-fatal, 8 cas	Descending Landry fatal, 17 cases	Bulbo-Pontine non-fatal 83 cases	Bulbo-Pontine fatal 19 cases	Cerebellar non-fatal 3 cases	Cerebellar fatal (none)	Encephalitic, non-fatal, 10 cases	Encephalitic, fatal, 4 cases	Meningitic, non-fatal, 7 cases	Meningitic, fatal, 2 cases	Abortive, 12 cases	Total No. of cases, 719
I. Fever	387	35	31	77	7	14	80	15			9	3	7	2	12	649
II. Gastro-Intes. (Nausea & Vomiting	144	11	12	37	1	8	27	1			7	4	3	1	4	260
(Constipation	111	8	10	24	5	6	18	9			1	1			1	194
(Diarrhea	28	6	2	4		1	4	2					1		1	49
III. Headache		7	6	26	1	2	10	4			1				4	61
(Twitching	14	1	2	3		2	5	3	2						1	33
(Restlessness	28	4	3	4		4	9	4	1				2			59
I.V. Nervous Symptoms (Irritability	2		1	2		1										6
(Delirium	2					1										3
(Stupor	1			6			2						1			10
(Convulsions	3			1			2				3					9
V. Sore Throat	9	0		4		1	3	1				1	1			20
(Coryza	12															12
VI. Respiratory Symptoms (Cough	12				2											14
(Sneezing	4	1					2	1							2	10
(Neck	6		1	2		1	6									16
VII. Pain (Back	13		2	2		2	1	1								21
(Abdomen	4				1											5
(Extremities	0													1		1
VII. Retention of Urine	3															3
IX. Sweating	2															2
X. Chills	3	1		3	1		2	1								11
History unobtainable	2			4												6
XI. Nose Bleed			1								1					2

Fig. 36.—Preparalytic symptoms.

above 104° F. The course of the fever was sustained in type with moderate diurnal variations. Lumbar puncture or intraspinal medication tended to modify the record by causing a reactionary rise in temperature. In most of the non-fatal cases the temperature reached normal by gradual decline on the sixth or seventh day of the disease.

The so-called abortive cases usually had a shorter febrile period. The so-called toxic cases, if they survived—and those which lived through the febrile period usually did survive—sometimes showed a longer febrile period, but uncomplicated cases which showed a longer febrile period than seven days were few. There were many cases which showed a longer febrile period, but these were the cases which had complications, which adequately and entirely explained the continuation of the fever. In the cases with chest involvement, lobar pneumonia, bronchopneumonia, and bronchitis were very common complications for obvious reasons, and in the non-lethal cases the temperature reached normal coincidently with the disappearance of the physical signs of such conditions.

Not only are these facts true of the continuation of the febrile period beyond six days, they are equally true of the exacerbations of fever which occurred. Intercurrent infections of all kinds, especially chest complications in cases with involvement of the respiratory muscles, often explained a sudden rise of temperature of variable duration at some period of the disease after the temperature had reached normal. Superficial infections, abscesses, or otitis media were sometimes the explanation; very often, as must be true in this class of patients where artificial feeding was used, a gastro-enteritis explained a sudden rise in temperature. These cases usually cleared up promptly under appropriate eliminative treatment. Frequently sudden rises in temperature immediately followed intraspinal or intravenous medication, and obviously were caused by such manipulations. A very significant fact is that in practically every case where there was a sudden rise of temperature a careful study failed to reveal any alteration in the clinical course of the disease or exacerbation of the paralysis. *I cannot recall a single*

Fig. 36.—Preparalytic symptoms.

case, either with or without exacerbations of fever, where the paralysis became more marked after improvement had begun. Certainly, if these rises of temperature were incident to the clinical course of the disease and part and parcel of it, one would expect it to be reflected in coincident changes in the pathologic processes and, therefore, in the clinical course of the disease.

Because of these facts we did not expect to find and were unable to find cases corresponding to Dr. Draper's "dromedary type."

A paralysis which tends toward increased destruction of function after improvement has been instituted should cause grave doubts as to the etiology being infantile paralysis.

Fever.—It will be seen that fever was the most common preparalytic symptom, being noted in 649 of the 710 cases where the history was obtained. Remembering that the history was given usually by the family, it may safely be assumed that fever as an early symptom occurred in practically every case.

Pulse.—In the majority of cases the pulse followed the temperature-curve and was proportionate to it. During the febrile period there was a rise of about 10 in the pulse-rate for every degree of fever. This, of course, is not at all distinctive, but is true of most febrile conditions.

There was a tendency in the majority of the cases for the pulse to remain disproportionately high for some days after the temperature had dropped to normal. In the ordinary case this occurred for five or six days. In the so-called toxic cases it was often very much longer.

This tendency for the pulse to remain elevated after the afebrile period may be true of certain other acute infections. Therefore I am unable to state at present whether or not this fact has any diagnostic importance.

Respiration.—During the febrile period the respiration rate in uncomplicated cases was proportionate to the temperature and dropped to normal coincidently with the temperature. The cases with chest involvement, of course, showed a rapid respiratory rate. Often a sudden rise in the respiration was an indication of chest involvement or a chest complication, such as

pneumonia or bronchopneumonia. Cases which developed acidosis had a rapid respiratory rate.

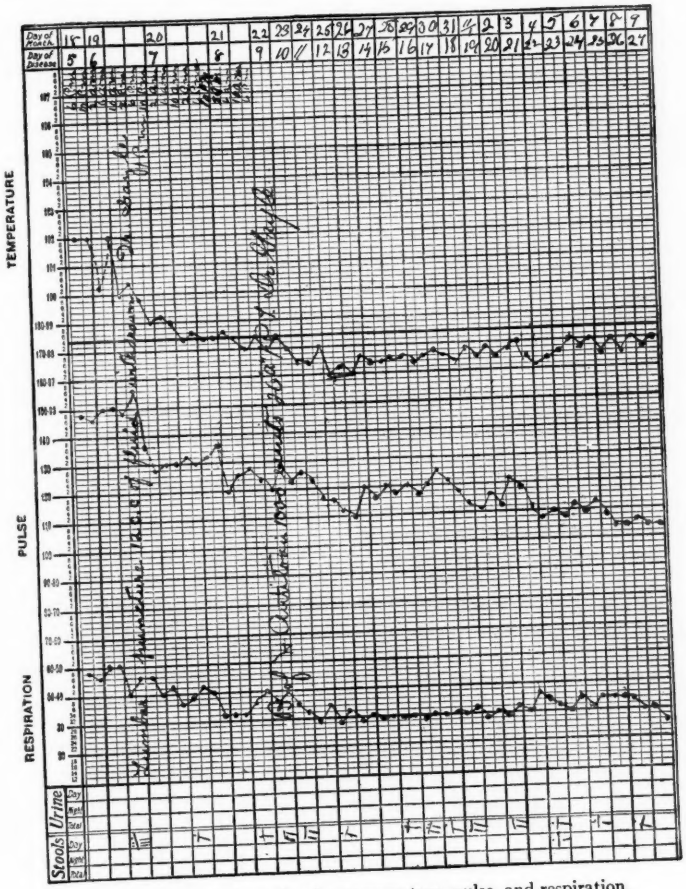

Fig. 37.—Typical chart showing temperature, pulse, and respiration.

Gastro-intestinal Symptoms.—Nausea and vomiting were observed in 260 cases; constipation in 194, being more common than is usually supposed; diarrhea was observed in 49.

Nervous Symptoms.—Twitching was seen in 31 cases, restlessness in 58, irritability in 6, delirium in 3, stupor in 10, convulsions were observed in 9. It is interesting to observe that 3 of the 10 hemiplegic (encephalitic) cases had convulsions. It is also worthy of note that many cases admitted during the epidemic with history of convulsions proved, on further study, to be some type of meningitis.

Respiratory Symptoms.—Sore throat was noted in 20 cases, coryza in 12, cough in 14, sneezing in 10.

Pain.—Headache was noted in 61 cases. Pain in the neck was noted in 16; in the back in 21; in the abdomen in 5, and in the extremities in 1.

Pain is probably a much more frequent symptom than this table indicates because most of the children are too young to express it. It was a very common preparalytic symptom in adults.

Retention of urine was noted in 3 cases. Objectively noted, it was much more frequent. Incontinence of feces was noted in 1 case, although constipation was more the rule than the exception.

Sweating was only observed as a preparalytic symptom in 2 cases. This is not in accord with the observation of Wickman and other observers.

Chills were present in 11 cases, rather a larger number than is usually observed.

Nosebleed was noted in 2 cases.

Objective Preparalytic Symptoms.—The number admitted in the preparalytic stage were relatively few. Practically all of these cases showed stiffness of the head and neck, with pain on motion. There was also rigidity of the back muscles and often retraction of the head. General hyperesthesia was usually present. In the preparalytic stage the reflexes were usually exaggerated, often Babinski and Kernig, ankle-clonus was not common. In other words, in most cases the preparalytic symptoms were those of meningeal irritation, and were indistinguishable from a true meningitis.

TOXIC CASES

A certain number of cases, not a very large percentage, were those which were obviously heavily infected. These were classified as the so-called toxic cases. The following types of cases were included under this heading:

(*a*) Cases where there was a very short preparalytic stage, characterized by a sudden onset, and a very rapid progression of symptoms.

(*b*) Cases where there was a very rapidly spreading paralysis, usually of the Landry type.

(*c*) Cases in which the above two types did or did not exist, but which were characterized by the fact that the appearance of the patient denoted profound intoxication. These usually had a very rapid pulse, a pulse disproportionately high to the temperature, and which tended to remain unduly rapid long after the temperature had reached normal.

(*d*) Cases which developed acetonuria and acidosis. It is a fact that many of these so-called toxic cases occurred in patients in whom there was cranial nerve involvement. Many of these cases had bulbar, pontine, or cerebral involvement.

ONSET OF PARALYSIS

With remarkable uniformity the paralysis came on about the second or third day, only rarely was it deferred longer, and there was a total absence of the old-time history of poliomyelitis, in which the child went to bed in a normal condition and awoke paralyzed. It was impossible to recognize absolutely the extent of the paralysis on admission of the patient to the hospital. This was because most patients were children around one and two years of age; second, because most of them were so sick that it was only possible to tell that a limb or limbs were paralyzed; lastly, because of the pain which accompanied manipulations.

PAIN

In the great majority of instances pain in the back of the head and neck with an accompanying rigidity came on about the same time that the paralysis appeared. Often the pain pre-

ceded the paralysis. As a rule it was possible in the early cases, even in the smallest children, to tell which limb was paralyzed by the fact that it was painful on manipulation. It was impossible to obtain a history of its onset or its presence in children, but in the adults who suffered from the disease the pain came on, in the majority of cases, after their admission to the hospital and after the paralysis had set in. Most of the adults described the pain as aching or sharp and shooting in character, the limbs being very tender to the slightest manipulation. In many instances the pain disappeared just as quickly as it came; many of the nurses, for example, while in the wards would point out a patient in whom the pain was present possibly in the morning, the child crying on manipulation, whereas in the afternoon of the same day there appeared to be no pain at all. The pain would last for about a week or two, and in the majority of instances it would subside gradually, and would be entirely gone when the patient left the hospital, that is, in about four weeks.

I am convinced that this pain is not at all of neuritic origin. I have tried to prove to myself that the peripheral nerves are diseased in infantile paralysis, yet in no instance did we find pain on pressure over the nerve-trunks at the time the pain was present. Sometimes I was under the impression that the muscles were tender to pressure, but I have come to the conclusion that the pain in poliomyelitis is entirely of meningeal origin, and that as the meningeal symptoms disappear, the pains also gradually subside. One point in favor of this view is the rapid subsidence of pain after lumbar puncture. Every patient on admission to the Municipal Hospital was given a lumbar puncture. These punctures were repeated as the occasion arose, according to the meningeal symptoms and the pain. Almost instantly after the lumbar puncture relief from pain and headache was obtained. In some of the cases whom we were fortunate enough to observe very early and in which lumbar puncture was done repeatedly, there was practically no pain present. As a result of all this I have come to the conclusion that Wickman's classification of the so-called neuritic form of infantile paralysis is an error, and that this type does not exist.

SPINAL FLUID

The residents who performed lumbar puncture directly after the patients were admitted to the hospital told me that in every instance the cerebrospinal fluid was increased in amount, this, of course, varying according to the type of case. As a rule, on lumbar puncture the fluid comes out drop by drop, whereas in infantile paralysis the fluid is more likely to come out with a gush and under great pressure, the amount varying from 15 c.c. to as high as 50 or 60 c.c. In some instances where lumbar puncture was done as often as every six hours there would be 20 to 30 c.c. obtained each time.

The residents called my attention to the fact that in those cases in which the paralysis was chiefly confined to the lower limbs the quantity of the cerebrospinal fluid was greater than in the other types of paralysis.

The following summary was kindly furnished me by Dr. Kolmer, who had charge of the laboratory work.

Summary of Findings in Cerebrospinal Fluid.—1. The majority of the fluids were water clear or showed but a faint opalescence against a black background; but 1 to 2 per cent. of blood-free fluids presented distinct turbidity. Xanthochromia and excessive fibrin formation were not found; about 10 per cent. of the fluids presented a small fibrin-coagulum after standing several hours.

2. Seventy-seven per cent. of the fluids from all stages showed an increase of total cells; in 80 per cent. of these the counts were not above 100 cells per cubic millimeter of fluid. An increase of the total cells was found in the preparalytic stage, and this increase was present in 80 to 84 per cent. of cases for at least two weeks after the onset of paralysis, when the decrease occurred.

3. In over 95 per cent. of fluids the small lymphocyte variety of cell predominated. Polymorphonuclear cells predominated in less than 1 per cent. of fluids, and in over 88 per cent. constituted less than 25 per cent. of the cells present.

4. An increase of globulin-albumin was found in 32 per cent. of fluids, and different tests for these proteins yielded varying

results. With the Noguchi test the fluid of 1 of 6 cases in the preparalytic stage yielded a positive reaction; the percentage of positive reactions then became gradually higher to the third week after the onset of paralysis (55 per cent. positive), when a rapid decrease in positive reactions became apparent.

5. During the acute stages the fluids of 40 to 50 per cent. of cases yielded a colloidal gold reaction of the luetic and meningitic zone types. All yielded negative Wassermann reactions. The balance of these fluids produced no precipitation at all, or but slight changes in the 1 : 10 and 1 : 20 dilutions.

6. The potassium permanganate reduction test yielded positive reactions of indices over 2.3, with the spinal fluids of 41 per cent. of cases examined from the second to twenty-first days after the onset of paralysis; a high reduction index indicates an increase of protein in the fluid and may aid, therefore, in the diagnosis of acute poliomyelitis.

7. Every fluid was found to contain sufficient dextrose to reduce Fehling's solution in some degree; partial reduction of the amount of dextrose was suspected with a number of fluids on the basis of a qualitative test.

8. Increased permeability of the meninges was indicated by the presence of natural antisheep hemolysin in the fluids of 66 per cent. of cases in the acute stages, and both the hemolysin and a hemolytic complement in 30 per cent. Both of these substances were absent in the fluids of control persons.

9. Substances inhibiting saponin hemolysis were not found in the fluids of cases two to twenty-one days after the onset of paralysis.

10. A definite and absolute diagnostic criterion or test with the spinal fluid in poliomyelitis has not been discovered. A clear or slightly opalescent fluid, poor in fibrin, reducing Fehling's solution and containing an increased number of cells chiefly of the mononuclear variety, are the most constant findings. An increase of globulin-albumin and a high potassium permanganate reduction index strengthen the diagnosis, while a colloidal gold reaction of the luetic and meningitic zone types and the presence of natural antisheep hemolysin are helpful diagnostic data.

EXTENT OF PARALYSIS

In the course of a few days it was possible to recognize the extent of the paralysis and the type of the disease. In the great majority the paralysis involved more than one limb. It may be

	Spinal, non-fatal 394 cases	Spinal, fatal 41 cases	Ascending Landry, non-fatal 35 cases	Ascending Landry, fatal 84 cases	Descending Landry, non-fatal 8 cases	Descending Landry, fatal 17 cases	Bulbo-Pontine, non-fatal 83 cases	Bulbo-Pontine, fatal 19 cases	Cerebellar, non-fatal 3 cases	Cerebellar, fatal none	Encephalitic, non-fatal 10 cases	Encephalitic, fatal 4 cases	Meningitic, non-fatal 7 cases	Meningitic, fatal 2 cases	Abortive 12 cases	Total number of cases 719
Neck	54	22	26	20	7	8	10	2				2	1			152
Chest	27	32	22	83	4	16	16	19				1				220
Back	49	4	3	3	1		4	1								65
Abdomen	9	5	2	9	1		3	1					1			28
r.arm	81	20	31	45	8	12	18	11			8	2	2			238
l.arm	84	21	30	44	8	14	17	12			2	3	3			238
r.leg	271	25	34	79	8	9	17	14	2		8	3	5	2		477
l.leg	280	25	35	76	6	10	18	14	2		2	3	6	1		478
5th nerve							2	2								4
3,4 or 6th	2						4	4	2							12
7th	1			1	1		66	18			10	4				101
9th & 10th							9	17				1				27
11th								1				1				2
12th							4									4

Fig. 38.—Location of paralysis.

said in the beginning that the extent of the paralysis in this epidemic was very severe. We have been accustomed in the past to seeing only a limb or part of a limb paralyzed, but certain it is that in this epidemic the infection has been very profound and the paralysis very great. As in former epidemics, the lower limbs were much more frequently involved than the upper. In only a few instances was one limb involved alone. In fact, I can recall only a few cases in which this was the case, although on discharge the paralysis in the majority of instances would be limited to one limb. It was not at all an unusual combination to find both lower limbs and one upper, and less commonly, both lower and both upper, implicated. Where the upper limbs were involved as in the lower, both were at first implicated.

TYPES OF PARALYSIS

In Wickman's[1] classification, which has been generally accepted, the following forms are distinguised:

1. The spinal poliomyelitis form.
2. The form resembling Landry s paralysis.
3. The bulbar or pontine.
4. The encephalitic.
5. The ataxic.
6. The polyneuritic (resembling neuritis).
7. The meningitic.
8. The abortive.

For all practical purposes this is a very good classification, but from my experience in this epidemic it would be well if the ataxic and the polyneuritic types were excluded altogether. As previously mentioned, in the Philadelphia epidemic I did not observe a single case which could be classed as polyneuritic.

Wickman (page 75) states that "although some undoubtedly belong to the bulbar type, there are many others in which the ataxia is not distinctly cerebellar in character and in which all signs of either bulbar or pontine indication are absent." From my observation there is no such thing as an ataxic type of poliomyelitis. There were a number of patients in whom there were distinct cerebellar symptoms, but in all with the exception

[1] Acute Poliomyelitis, Nervous and Mental Disease Monograph, Series No. 16.

of one they were in association with pontile lesions. Therefore, if such classification is to be made, the cerebellar type would be much more appropriate than the ataxic.

Spinal Form.—By far the commonest form of infantile paralysis is the spinal type. This is especially true in the non-fatal cases. There is one essential difference between fatal and non-fatal spinal cases, and that is that in the former the chest is almost always implicated, death resulting from respiratory paralysis, whereas in the non-fatal types the chest is less frequently affected.

Landry Type.—The so-called Landry type of paralysis is by no means as distinct as is commonly supposed to be the case, for in many instances it is impossible to distinguish it from the spinal type. The Landry type of paralysis is, of course, most commonly present in the fatal cases, and in these the paralysis progresses so rapidly, death nearly always occurring on the second or third day, that in many instances it is only by a stretch of the imagination that one can distinguish either the ascending or descending Landry types. There are, however, undoubted cases in which there is an ascension and descension of the paralysis. The ascending type is by far the most common.

Of 168 deaths, 84 were the result of the ascending type, 17 of the descending type, of Landry paralysis. In 41 death was supposedly the result of spinal form of paralysis, but in practically all, whether Landry or spinal forms, death was the result of respiratory involvement.

Ascending Landry Type.—In the ascending Landry type the paralysis almost always begins in one or both lower limbs and rapidly ascends and involves the abdomen and chest, causing death by respiratory failure in the course of two or three days. At times only one lower limb is involved with the chest, but in the usual case both lower limbs and chest are implicated. More rarely one or both shoulders are also paralyzed, and in the more severe cases the whole of the upper limbs with the chest and neck. In some the paralysis is very rapid. In one case the whole course of the disease was only twenty hours. In these the children become stuporous from the beginning.

Descending Landry Type.—In the descending Landry type the paralysis nearly always begins in the neck and then takes in the chest often alone, but chiefly in combination with one or both upper limbs. In most of the cases the lower limbs are not at all involved. Because of the neck paralysis the head cannot be lifted up, there is, of course, restriction of respiration, and in the upper limbs the shoulders are principally involved. In those cases in which the lower limbs are not involved the reflexes are frequently exaggerated, Kernig's sign is present, and there is rigidity of the lower back. Frequently with the increase of the tendon reflexes in the lower limbs there is a Babinski which is dependent upon the meningitic symptoms and the increase of spinal fluid. Death usually is very rapid, occurring on an average of about the third or fourth day after the onset of the first symptoms.

Types of Paralysis.—*Lower Limbs.*—The muscles involved with the greatest frequency were those of the pelvis and thigh, especially the quadriceps and adductor groups, and more rarely those concerned in abduction and flexion of the thigh. Of the muscles below the knee, the anterior tibial group was more frequently involved than the peroneal.

In a great majority of cases in which the entire limb seemed paralyzed motion could still be obtained in the toes, especially in flexion, less frequently in association with the movement of the toes the ankle could be moved. It was only in the fatal cases that complete paralysis of the lower limbs without any motion was obtained, although there were occasional non-fatal cases in which this was also true.

Muscles of Trunk and Abdomen.—The abdominal and back muscles were very frequently involved. The former was manifested by an absence of the abdominal reflexes and a laxity of the abdominal muscles, often with great distention, which was not dependent upon an atonic condition of the intestines or distention of the bladder. Rarely the abdominal muscles were paralyzed only on one side. The weakness of the back muscles, that is, a weakness of the lumbar and trunk muscles, was manifested by an inability on the part of the patient to sit up. It can,

as a general rule, be said that the weakness of the abdominal, lumbar, and back muscles was generally overlooked, especially in the beginning of the disease, in which it was impossible to allow the patient to sit up. After the recession of paralysis it was frequently found that in addition to what was thought to be a paralysis only of the lower limbs, there was also considerable involvement of the back and abdominal muscles.

Upper Limbs.—In the upper limbs the shoulder group was predominantly involved. Only in a few instances were the fingers and hands also implicated. There were a number in which besides the shoulder paralysis there was an implication of the upper arm group, and more rarely of the muscles below the elbow. In comparison with the lower limbs it can at once be stated that not only were the paralyses of the upper limbs less frequent, but they were very rarely as complete.

There were no instances of paralyses in the upper limbs without involvement of the shoulder group, while in the lower limbs there was rarely implication of the muscles below the knee without other paralyses. In the beginning of the paralysis of the upper limbs it was not at all infrequent to see the weakness begin in the shoulder and then involve the muscles of the upper arm, forearm, and hands, but with the exception of a few instances when the patient left the hospital the paralysis was limited to the shoulder.

Regarding the method of onset of the paralysis in the upper limbs, the first weakness was always present in the shoulder group and rapidly extended downward. There was no instance in which the paralysis began in the lower part of the limb and ascended upward. This is borne out also in the Landry type of paralysis, in which quite frequently in the ascending Landry type there would be rapid ascension of the paralysis from the lower limbs to the abdomen and chest muscles to the shoulders, and then to the muscles in the more distal portions. Frequently in the ascending Landry type the shoulders would be involved alone without implication of the parts below. Rarely both in the ascending or descending Landry type the shoulder muscles would escape entirely. This is important because it has been

claimed that in the Landry type of paralysis the progression of the paralysis is longitudinal in direction.

In the progression of the paralysis in the lower limbs the same thing was noticed as in the upper, that is, the paralysis began in the proximal portions, in the muscles of the pelvis and thigh, and extended distally. We have no record of a single instance in which the paralysis started in the parts below the knee and extended upward.

Neck Muscles.—Weakness of the neck muscles was quite frequent. This was especially true in the descending Landry type and in the bulbar cases, and more rarely in the spinal type. Such weakness is manifested by an inability on the part of the patient to lift the head. Unilateral neck weakness was occasionally present.

Chest Muscles.—In the fatal cases the chest muscles were almost invariably implicated, the progression of such involvement being the cause of death, In the non-fatal cases, however, especially in the spinal type, the chest muscles were not so frequently implicated.

RECESSION OF PARALYSIS

Certain definite facts can be gathered regarding the recession of the paralysis.

There was not a single case in which the paralysis increased after improvement had been initiated. This, I believe, is of the greatest importance, for there have appeared statements in the literature of delayed and recurrent cases in the same attack.

Facial cases cleared up with considerable rapidity. This was true of the peripheral type. It was not equally true of the facial palsies which were a part of a hemiplegia. Regarding paralysis in general, it may be said that the limb first affected was usually the most extensively involved, and at the time of the patient's discharge was the one most extensively paralyzed. This may mean one of two things: Either that the limb first affected was most extensively involved, and therefore recovered more slowly, or that although the rate of recovery was the same, there had been greater and more prolonged destruction, and

therefore there appeared to be greater involvement at the time of discharge. Regarding paralysis of the extremities, it may be said that paralysis of the arms cleared up more rapidly than paralysis in the legs. I mean that the actual rate of improvement was greater in the arms.

Distal muscles of any particular extremity cleared up more rapidly than the proximal muscles. Perhaps here the rate of improvement was the same because, as a rule, the proximal muscle groups were first and most extensively involved. Therefore, when improvement did occur it would manifest itself to a greater degree in those muscles least affected.

I believe, therefore, that the rate of improvement *in any given extremity may be the same, but that there is a more rapid improvement in the upper extremities when contrasted with the lower extremities.*

In those cases which survived, cranial nerve palsies disappeared rather promptly, vocal cord paralysis or deglutition paralysis in non-fatal cases clearing up in a few days.

Cerebellar cases cleared up promptly. Cerebral hemiplegias not so promptly.

We observed one case of incontinence of feces, but constipation was rather the rule and tended to be persistent. It was often associated with absence of the abdominal reflexes, and therefore we thought it possibly dependent on a deficiency in expulsive power. We cannot exclude the possibility of pathologic processes involving the plexuses of the vagus and sympathetic.

In cases in which the abdominal reflexes were absent there was a tendency for them to reappear during the child's stay in the hospital. This was true of all superficial reflexes. It was not at all true of the deep reflexes.

THE TONICITY OF THE LIMBS AND REFLEXES

It is needless to say that the paralyzed limbs in infantile paralysis are flaccid and that the reflexes are lost in the involved parts. Frequently, however, the limbs are found to be rigid and the reflexes prompt, and it was not at all unusual to obtain ankle-clonus and the Babinski phenomenon. Whenever in a

paralyzed limb there was found a hypertonicity and ankle-clonus or the Babinski phenomenon it was almost always the result of a meningeal complication and an increase of cerebro-spinal fluid, for almost invariably with lumbar puncture the hypertonicity, clonus, and Babinski disappeared. The Babinski phenomenon, of course, was present and persisted in a number of cases on their discharge from the hospital, but in these it was undoubtedly due to an involvement of the lateral columns. This, however, was by no means common.

Wickman in discussing the state of the reflexes and tonicity of the limbs remarked upon the variability of the reflexes. On page 48, in discussing alteration of the knee-jerk, he makes the following five classifications:

1. Absence of the knee-jerk is the rule. It is noteworthy that the loss of the patellar reflex may be the only demonstrable objective sign of the disease (Wickman, Ed. Müller, Zappert).

2. An initial increase with subsequent disappearance may occur (Wickman, Ed. Müller).

3. If the arm is affected, or if the bulb be implicated, an otherwise normal leg may show an increase of the patellar reflex (Wickman, Neurath, Zappert, Foerster, Ed. Müller).

4. Paralysis and loss of reflexes in one leg may be associated with apparent healthiness and increase of reflexes in the other (Wickman, Zappert).

5. The patellar reflexes may be increased in a paralyzed and obviously atrophied leg (Wickman).

Then he stated that these variations cannot be to a certainty interpreted. He thought, however, that the initial increase and the subsequent diminution may be explained by supposing that in the early stages of the disease the inflammatory process increases the irritability of the spinal cord, and that as the disease advances the stimulation gives place to the destruction of the nerve-cells, and the irritability diminishes and the reflexes disappear. He then gives further examples in the variations of the reflexes and quotes the experience of other observers.

These expressions of opinion are, of course, very interesting, but it is probable that in no epidemic was the lumbar puncture

needle so freely used as in this. With the appearance of any meningeal symptoms of ankle-clonus, or the Babinski phenomenon or of pain, lumbar puncture was done, with an almost prompt disappearance of these symptoms, and I came to the conclusion that whenever there was an alteration of reflexes from what was to be expected, from the nature of the neurologic lesion, it was because of the attending meningitis and the increase of cerebrospinal fluid. Many articles on this disease and many textbooks and manuscripts discuss the early increase of reflexes and early hypertonicity. This is the result of the meningitis and increase of spinal fluid, as can be readily proved by lumbar puncture. These statements are true not only of the knee-jerk, but of other tendon reflexes in both lower and upper limbs.

Mention is mde by Wickman, who also quotes Lindner and Mally, page 49, of the disappearance of the superficial reflexes and of the preservation of the abdominal reflexes even in pronounced paralysis of the abdominal muscles. This was not substantiated by our investigation. Wherever the abdominal muscles were involved there was always an absence of the umbilical reflexes and sometimes the epigastric reflexes. The same can be said of the cremasteric reflex.

BULBOPONTINE CASES

It is apparent that the bulbopontine classification of Wickman can be divided into six groups:

1. Bulbar.
2. Pontine.
3. Pontine bulbar.
4. Pontine spinal.
5. Bulbar spinal.
6. Pontine bulbar spinal.

Bulbar.—Throughout the epidemic a great many so-called bulbar cases were reported, and it was the impression that most of the deaths were the result of such involvement. As a matter of fact, this was not at all so, for of the 168 deaths, in only 26 was the medulla implicated. Of these there were only 2 undoubted cases in which the disease was entirely limited to the medulla

oblongata. In both there was difficulty in swallowing, with regurgitation of food, with no evidence of paralysis of the limbs, but with increase of the reflexes because of the general meningeal involvement. There was also another patient who had difficulty in swallowing, but examination of the pharynx denoted no paralysis, and there was also no fever and no increase in cerebrospinal fluid. There were a number of such cases throughout the epidemic in which the differential diagnosis was very difficult, that is, patients in whom there was only difficulty in swallowing or in breathing, without palatine laryngeal or pharyngeal paralysis, but which were called poliomyelitis. I cannot conceive of this disease limiting itself to only one function, that is, swallowing or breathing, without at the same time other evidence of organic involvement. I have no doubt that these patients died from some other cause, but, as is well known, during epidemics all sudden deaths are attributed to the predominating disease.

The usual bulbar symptoms consisted in difficulty in swallowing; occasionally when there was not so much difficulty there was also regurgitation of food. In other cases there was only a nasal twang to the speech, although this at times accompanied difficulty in deglutition. It is interesting that bulbar symptoms were often either the beginning or termination of the Landry type of paralysis.

Pontine.—There were 22 instances in which the facial nerve was involved alone. Of these, the right face was involved 13 times and the left face 9. In 5 there was accompanying rigidity of the neck, and in 1 increase of reflexes with slight Babinski due to meningitis. In only 1 case did death occur, and in this patient it occurred on the twentieth day as the result of gastroenteritis.

Pontine Bulbar.—There were 24 instances of pontine bulbar involvement. Two fatal and 22 non-fatal. In both fatal cases death occurred due to involvement of the tenth nerve because of inability to swallow, and, in addition, in 1 case there was involvement of the face on one side and in the other on both sides.

Pontine Spinal.—Of this type there were 46 cases, 36 non-fatal and 10 fatal. It is interesting that in the non-fatal cases

the only cranial nerve involvement was that of the facial nerve. In one patient the facial nerve was involved on both sides. The limbs were involved with about equal frequency. Of the 10 fatal cases, in all with the exception of 1 the facial nerve was involved. In one the sixth nerve was also implicated, while in one other the sixth nerve was the only cranial nuclei diseased.

Bulbar Spinal.—There were 12 altogether, 4 non-fatal and 8 fatal. In all, with the exception of 1 non-fatal case, the ninth and tenth nerves were involved, causing either difficulty in swallowing or in talking. In one very interesting case the eleventh nerves were involved in either side, this being a very unusual and, of course, rare occurrence. The limbs and chest were involved with equal frequency.

Pontine Bulbar Spinal.—Of this variety there were 14, with an equal number of fatal and non-fatal cases. In 3 of the non-fatal variety the motor ocular nerves were involved three times; the fifth, twice; the seventh, in all; the ninth and tenth, five times, and the twelfth, twice. Whereas in the fatal cases the ocular motor nerves were involved twice, the fifth twice, the seventh five times, the ninth and tenth in all cases, this being the cause of death.

UNUSUAL BULBAR CASES

There were a great many unusual cases in which there was not only implication of the medulla and pons, but also of other portions of the brain in addition to spinal cord involvement. There was one patient two months old in whom there was involvement of the right face, difficulty in swallowing, weakness in all the limbs, and conjugate deviation of the eyes due to cortical implication. In another patient, a girl of three, there was a bilateral third nerve involvement, as shown by the unequal pupils and sluggish reaction, bilateral fifth nerve palsy, ninth and tenth nerve paralysis, as shown by the inability to swallow and talk, with weakness and atrophy of the right twelfth nerve. In addition, there was a right hemiplegia. In another patient aged three there was a right motor fifth, sixth, and seventh nerve paralysis with involvement of the ninth and tenth nerves. There was also, in addition, left sixth nerve paralysis and left twelfth nerve palsy

and weakness of the muscles of the neck. In another boy, aged four and one-half years, there was involvement of the left seventh and sixth nerves, weakness of the neck muscles, and of both lower limbs, with lost reflexes and Babinski phenomenon. There was also one very unusual patient eighteen years of age, who had, besides involvement of the left limbs, right motor and sensory fifth nerve paralysis with a right seventh nerve palsy, sensory involvement of any part of the body being extremely uncommon.

The conclusion is evident that the seventh nerve is the commonest of the motor cranial nerves to be implicated, next in frequency is to be found the sixth, then the ninth and tenth, motor fifth, third, and twelfth.

OCULAR CASES

These were not at all uncommon, for, as has been mentioned, sixth nerve palsies frequently developed as a complication of other forms of bulbar paralysis. There was one instance of a bilateral sixth nerve palsy with no other paralysis with the exception of a general increase of reflexes. Another patient had both sixth with the right seventh nerve paralyzed with a slight involvement of the chest. Then there was a colored boy with paralysis of associated ocular movement to the right and left, in addition to a right motor fifth paralysis with a right hemiplegia. Another boy had complete external and internal opthalmoplegia. Another patient had conjugate deviation of the eyes to the right, and there were 4 or 5 with nystagmus in different directions. Besides, there were 3 instances of ptosis of one or both upper lids, and 2 cases in which there was difference in the size of the pupils due to spinal lesions. Optic neuritis or atrophy was not found.

CEREBELLAR CASES

There was one patient in whom the cerebellum alone was implicated. This was a child of five who had marked asynergy in all of the limbs and trunk, with the usual cerebellar trunkal gait and symptoms. Gradually these cleared up and in about twenty days they entirely disappeared. There were 4 other

cases in which there were accompanying cerebellar symptoms. In one, a child of three years, there was undoubtedly implication of the posterior portion of the cerebral crura, for there was bilateral ptosis, oscillations of the eyeballs, jerkings over various portions of the body, with asynergy of the limbs. This was no doubt due to the implication of the superior cerebellar peduncles and the third nuclei. In another patient in which the lesion probably had a similar location there was ptosis of both eyelids, slow oscillatory nystagmus to the right, cerebellar gait, and asynergy of all of the limbs. The symptoms disappeared in about twenty days.

ENCEPHALITIC TYPE

There were 4 fatal and 10 non-fatal cases. Usually the symptoms were preceded by convulsions followed by hemiplegia of the same side. The paralysis had the usual characteristics of a cerebral lesion, that is, increased reflexes and Babinski. In addition, in 5 instances there was implication of the spinal cord. Again, there were meningeal complications which caused temporary increase of reflexes and Babinski on the non-paralyzed side.

MENINGITIC GROUP

Practically all cases of infantile paralysis have a certain amount of meningeal involvement. From the beginning the children complain of pain in the head, neck, and back, and sometimes a general pain which causes them to scream at the slightest touch. In these cases, even in the mildest, early after the onset there is always a certain amount of rigidity of the head and neck. This rigidity can be easily seen and felt not only in the back of the head and neck, but throughout the whole extent of the spine. Of course this varies according to different cases. As has been previously mentioned, the pains are always more marked in the paralyzed limbs.

There were, however, undoubted cases in which there was meningitis alone and in which this was the most prominent symptom. In some there was a passive weakness of the neck muscles or possibly of the shoulder or one or both lower limbs, but, as a rule, where the meningitis was very great the paralysis

was not very marked, and on the subsidence of the meningitic symptoms there was very little remaining paralysis. This was so common that the prognosis in meningitic cases was always pronounced better than in other types, although 2 deaths occurred in such cases from infantile atrophy. Three distinct types were noted. The most common was that in which there was present the usual symptoms of a general meningitis. There were, however, what I call the upper and lower type of meningitis. In the so-called upper types there was retraction of the head and neck with marked rigidity and stiffness of the upper limbs, the lower part of the back and both lower limbs being flaccid. In the lower type the head and neck and upper limbs and upper spine were normal, but the middle and lower spine were rigid, the thighs flexed on the abdomen, legs on thighs, with Kernig's sign, and marked rigidity and resistance whenever either of the lower limbs were moved.

In all of these instances there was a marked increase in the cerebrospinal fluid, and punctures performed daily or at more frequent intervals always give an increase of the amount of fluid. Meningeal cases usually subsided in the course of a week or ten days.

ABORTIVE TYPE

There were about 12 abortive types admitted, the symptoms consisting of the usual fever, vomiting, headache, constipation or diarrhea, followed by rigidity of the head and neck and occasionally of the back. Often the meningitic symptoms were marked, the limbs being rigid, there being present besides a general increase of reflexes, Kernig's sign, and Babinski phenomenon. Lumbar puncture always showed an increase in the quantity of the cerebrospinal fluid with the usual findings. Occasionally weakness was present in one or both limbs, but of a fleeting character. The fever never lasted more than four or five days, the pulse-rate was never very great, and the respiratory rate was never increased. The whole course of the disease never lasted more than a few days and paralysis never followed.

It is, of course, impossible in any epidemic to obtain the exact number of so-called abortive cases because most of them do not

come under observation or are unrecognized. In this work two physicians investigated a number of the wards in Philadelphia with a view of finding out if possible the frequency of such cases. The results were altogether at variance, but some deductions can be made from the work of these physicians. In one investigation in which the houses of 155 frank paralytic cases were investigated there were found 10 instances in which the disease appeared in more than one child and 34 abortive cases. In other words, in addition to the paralytic cases there were 21 per cent. abortive types. This percentage may be high, yet it is quoted for what it is worth.

MULTIPLE CASES

Of the cases admitted to the hospital, in 14 there were 2 members of a family with the disease. In all but 2 the disease came on within twenty-four hours, in the 2 it came on within seven days of each other. In our extra hospital investigation 10 multiple types were discovered out of 155 frank cases. If this ratio were accepted, then the number of multiple cases must be indeed very large. It was evident, however, that in practically all the disease appeared within one or two days, and this at once argues against contagiousness of infantile paralysis, for the period of incubation has been generally placed at from five to eight days.

RECURRENT CASES

In the September number of the Journal of Nervous and Mental Diseases E. W. Taylor reported an undoubted case of recurring infantile paralysis. One such case came under my observation.

This patient at the age of four began with fever, intense diarrhea, and paralysis of both legs on the third day. Dr. Kelsey attended the child at this time thirteen years ago. The onset of the symptoms and the paralysis was such that he diagnosed it as a case of poliomyelitis. At any rate, the child was paralyzed in the lower limbs and in bed for four weeks, the lower limbs regaining their full power in the course of about six months. The present attack thirteen years later occurred in July, with

headache, fever, pain in the back of the head and neck, and about three days later paralysis of both legs, buttocks, and lower abdomen appeared. She was taken to the Municipal Hospital and was discharged on August 25th. When examined by me with Dr. Kelsey she had a marked involvement of the pelvis, thigh, and some of the leg muscles, with the usual flaccid condition and loss of reflexes.

The only question about this being a recurrent case is the fact that after the first attack there were no remaining paralyses, and yet, judging from our experience in this epidemic, this is not at all unusual. There is no question that the child was totally paralyzed in the lower limbs at first, with a gradual recovery of power at the end of six months. Besides, we have Dr. Kelsey's word that she probably was a case of infantile paralysis. These cases, of course, are very rare, but that they do occur Dr. Taylor's case and those he quotes undoubtedly prove.

As the result of the study of these cases I have made the following modification of Wickham's classification of poliomyelitis:

1. The spinal form.
2. The form resembling Landry's paralysis.
3. The pontine bulbar:
   - (*a*) Bulbar.
   - (*b*) Pontine.
   - (*c*) Pontine bulbar.
   - (*d*) Pontine spinal.
   - (*e*) Bulbar spinal.
   - (*f*) Pontine bulbar spinal.
4. Encephalitic.
5. Cerebellar.
6. Meningitic.
7. Abortive.

CASES SENT TO THE MUNICIPAL HOSPITAL AS POLIOMYELITIS, BUT IN WHICH THE DIAGNOSIS WAS INCORRECT

There were 37 such cases. Of these, 10 were instances of cerebrospinal meningitis, 6 tubercular meningitis, 6 pneumonia, and of the other miscellaneous diseases there were 2 who had

meningitis resulting from chronic otitis media, 2 with scurvy, 1 with scarlet fever, 1 with tetanus, 2 with contusions of the hip and knee, 2 with hemiplegia, 1 with neuritis, and there were 4 in which no diagnosis could be made.

QUESTION OF CONTAGION

I started out with the idea, after having read Wickman's and Römer's articles and from the New York reports, that the disease was personally contagious, but the more experience I had the more I got away from that impression. Of the multiple cases, in all but 2 the symptoms in the second case appeared within one or, at the most, two days. Unless, therefore, it is argued that the period of incubation is one or two days, it must be admitted that there must have been a similar source of infection. Second, in our field study of the abortive types the evidence indicated that they appeared at the same time as the frankly paralytic cases or within one or two days, again pointing to a similar source of infection. Third, of the cases which were admitted to the hospital, but which turned out to be other than poliomyelitis, not a single one developed the disease. Fourth, there is no instance of any nurse or physician who either acquired the disease or who carried the disease elsewhere. A number of the attending physicians with young children in their families went home daily and did not carry the infection with them. I have no doubt that many more such examples occurred in New York. It was the impression of all the nurses and physicians that poliomyelitis was not spread by personal contact, meaning by that that it is not spread in the way that measles, scarlet fever, or whooping-cough is. If, however, such a possibility is admitted, it must be that the second person must come in contact with some of the excreta, such as saliva, etc. It might be interesting also to consider in this connection that in the Municipal Hospital are housed all the contagious disease, such as scarlet fever, diphtheria, etc., and that the attendants and nurses of the various units lived together, and yet, there was only one instance in which a child in any other department (scarlet fever) developed poliomyelitis.

One very striking example of the non-contagiousness of the disease was furnished us in Chester County, near Philadelphia. There is in Cedar Hollow a stone quarry in which Italians work. There is a row of ten tenement houses in which live about 60 Italians, 40 of which are children, most of them under six years of age. The water-supply was contaminated. Each family had its pigs and dogs and the sanitary conditions were beyond belief. Two instances of the disease appeared about the same time in two families living in separate houses. There was also another case about one-half mile away in an Italian family. As is customary with these people, all of the other children and adults visited the sick children before the inspector had the opportunity to pronounce the disease poliomyelitis, indeed, he did not take the trouble to quarantine them because he knew the rules could not be enforced. Here was every opportunity for the disease to spread, and yet investigation by the local inspector, Dr. Mills, and myself showed that not only were there no other cases of the disease, but there were not even abortive cases.

TREATMENT

The cases admitted during June, July, and August all received urotropin. In these cases lumbar puncture was done only for diagnosis and was seldom done more than once. Most of the cases admitted in the latter part of August and in September, October, and November had repeated lumbar punctures for therapeutic as well as diagnostic purposes. Many of these cases received intraspinal injections of adrenalin chlorid 1 : 1000, immune serum, normal serum, one, or both, or all under various conditions.

It is entirely impossible to draw deductions regarding the efficacy of treatment from statistics of cases.

Many extremely ill patients survived and made a good recovery without lumbar puncture or any intraspinal therapy, and many patients apparently not so ill died despite any or all of these procedures.

But one cannot help but form certain impressions from a study of a large group of cases.

Certainly if any treatment avails, it can best be judged by its use in the preparalytic stage. It is our belief that in this stage prompt and frequent lumbar puncture is valuable for the mechanical relief of pressure and for symptomatic relief. For example, in a boy of fifteen seen in the preparalytic stage with great stiffness of the neck, spinal tenderness, and severe headache, following prompt lumbar puncture, where 50 c.c. was removed under great pressure, there was within five minutes a total relief of headache and rigidity of the neck, and these symptoms never recurred throughout the entire subsequent course of the illness. Whether or not lumbar puncture has any value in lessening the ensuing paralysis I am unable to state, I do not believe it is of any value in the absence of pressure and meningitic symptoms. In other words, I do not believe it is of any value after the case has reached the stage of absent reflexes, flaccidity, and paralysis. The persistence or recurrence of meningitic symptoms is an indication for its immediate and frequently repeated employment.

Intraspinal Adrenalin.—This was used, as advocated by S. T. Meltzer, in a considerable number of cases. I am not sure of its value. We do not believe that there has been any conclusive evidence to show that it has any effect on influencing the course of the paralysis. Possibly recovery of function after damage has ensued may be hastened by its use. Quite a few cases reacted badly following its use, especially after the second or third injection. In these cases it was considered wise to discontinue it entirely.

Immune Serum.—As is true of all therapeutic procedures, the value of this one can be best judged in the preparalytic cases. For example, a boy aged six was seen in the early preparalytic stage, as evidenced by meningitic symptoms and exaggerated reflexes. Immune serum was used immediately, both intraspinally and intravenously. Despite this the child succumbed to a typical ascending Landry type of paralysis, dying seven hours later from intercostal and diaphragmatic paralysis. Of course conclusions cannot be drawn from a few cases. This case is cited because it seems to be especially appropriate.

We do not believe that immune serum as used has proved to

be of value. Possibly it should be used in very much larger doses than have been employed by us. This is certainly worth trying.

Various other agents were used at different times, among which may be mentioned urotropin by mouth, normal serum (intraspinally and intravenously), mercuric chlorid solution (intraspinally), and solutions of arsenobenzol intravenously. We are not convinced of the value of any of these agents.

CLINIC OF DR. O. H. PERRY PEPPER

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ESSENTIALS AND LIMITATIONS OF AN AVERAGE DIET

IN the course of this short series of clinics on the diseases of the gastro-intestinal tract reference has frequently been made to various questions of diet, and so in this final hour it seems proper to consider this subject a little more in detail.

We have more than once loosely spoken of faulty diet, and have attributed certain cases of gastritis and constipation as being due at least in part to this cause. On such occasions we have had in mind faults of cooking or of digestibility rather than faults of caloric value or of metabolic sufficiency.

It is easy to speak of dietary faults and of an ideal diet, but it is a very different and difficult matter to define what one means by an ideal diet. Much controversy has arisen over this point, and many fads have appeared, the followers of which have continued to maintain life and health despite the gloomy prognostications of their opponents. Diets have proved to be adequate which did not approximate the minimal requirements set down by some writers, and, on the other hand, theoretically adequate diets have failed in practice.

Today we are, however, facing conditions which make all details of food supply and utilization of interest, and it is possible that many questions of dietary insufficiency may become of immediate importance.

As has been said, it is difficult to directly define an ideal diet, but perhaps by observing the recognized results of diets known to be faulty we may gain a clearer view of the essentials of a satisfactory and adequate diet and its limits in the direction both of deficiency and excess.

Before we consider the individual constituents of an average

diet let us first discuss the questions of its caloric value and total bulk.

Caloric Value.—An average diet for an average adult of about 150 pounds in weight contains about 2500 calories, and this is generally accepted as sufficient for an adult under conditions which demand but little physical work, as, for example, an office worker. But just as soon as muscular work is done the caloric intake must rise, and figures have been obtained under conditions of exceptional exertion averaging as high as 8000 (college football team in California, 7885 calories per day per man). Many other figures for men doing hard work show no such excessive diets, as, for example, the Yale University Crew at New Haven, 3705; and the Harvard Crew at Cambridge, 4130. The caloric intake is, therefore, in almost direct relation to the muscular work of the individual, and a diet too rich in calories can only be considered so with a full knowledge of the activities of the individual. The results of the continued use of such an excessive diet depends, of course, to some extent upon the form in which the diet is taken, but in general it may be said that obesity will result. During the period of growth, however, a high diet is almost essential, and such figures as those obtained at St. Paul's School by Gephart are probably not very uncommon. Among that group of growing boys an average calculated caloric value of food for the twenty-four hours of 5000 calories was found, of which 14 per cent. was from protein. This represents about 210 grams of protein.

On the other hand, a calorically insufficient diet must lead sooner or later, depending upon the degree of insufficiency and the reserve stores of the body, to a gradual starvation. And here again it must be remembered that the nature of the deficiency will often be more important than the mere lack of total calories. Rubner considered 2000 calories desirable for a monk in retirement, but this figure is much higher than the average intake of many more active individuals, and the physiologic demands of an average adult may perhaps be as low as 1000 calories. On such a minimal intake, however, the individual sacrifices his reserves and loses much of his resistance and stamina.

We may, therefore, put down as the first requisite of our diet that it should contain at least 2000 calories and not over 4000, unless as a result of unusual demands in the nature of excessive muscular exertion.

Bulk.—In addition to the constituents protein, fat, and carbohydrate, and the relative part played by each in the diet, the total bulk is worthy of consideration. This will vary, of course, not only with the actual amounts of protein, fat, and carbohydrate, but also with the percentage in which each occurs in the food substances employed. Thus, for example, an average diet of 100 grams of protein, 400 grams of starch and sugar, and 50 grams of fat yielding about 2500 calories, will have an average weight of about 1400 grams, and will supply sufficient bulk to call forth salivary secretion by necessitating mastication and also gastric secretion by mechanical filling of the stomach. Furthermore, such a diet will, in all probability, produce a sufficient residue or roughage to assist the colon and lower bowel in its function by forming sufficiently bulky feces. The vegetarian, on the one hand, however, suffers from the necessity of taking his food in too bulky a form, for whereas the meat eater can obtain his protein as 20 per cent. of lean meat or 85 to 90 per cent. of dried meat, the vegetarian must rely on the pulse foods, such as peas and beans, in which protein is present in not over 6 per cent. in the fresh and 25 per cent. in the dried form. Furthermore, the total bulk is further increased by the fact that in a vegetarian diet there is a loss by failure to digest and assimilate fully 20 per cent. of the vegetable protein as compared to a much more complete utilization of the proteins of a meat diet. Furthermore, the majority of vegetable proteins are incomplete, as will be pointed out later, and so a greater total amount is required. Thus, the vegetarian must eat a very bulky diet not only because his food-stuffs contain a low percentage of protein, but also because their vegetable proteins are less useful and also less available. Whether such a bulky diet with its large undigested cellulose is harmful is unknown, but it is certain that a diet which errs in the opposite way may produce definite disturbances.

On the other hand, it is impossible to reduce the bulk of the solids of an average diet such as we have detailed above (protein, 100 gm.; carbohydrate, 400 gm.; fat, 50 gm.—2500 calories) to a smaller compass than about 386 c.c., or roughly, ¾ pint. This mass would weigh about 550 gm., and would be represented by 1700 5-grain pills. It would be necessary to add to this mass of solids almost 3 liters of water before it could be digested. Attempts to reduce this bulk still further must result either in the omission of some part or serious interference with the digestibility by excessive desiccation. Perhaps as important as the actual reduction in total bulk is the lack in such concentrated diets of an indigestible cellulose residue. Too little residue is a frequent cause of constipation and its associated disturbances. Finally, but not of least importance, is the fact that a greatly concentrated diet is seldom palatable, never encourages mastication, and usually results in faulty digestion and absorption.

Water.—Closely related to the question of total bulk is that of fluid intake. As a rule this varies greatly in different individuals and under different conditions. This must needs be if a water balance is to be maintained. For example, water leaves the body in the urine, feces, sweat, expired air, and to a trifling extent in other secretions. The feces may account for over 100 c.c., and the loss of water through the skin and lungs may vary from 1 to 8 liters, while the urinary output stands in relationship to the total water intake and the amounts lost by the other channels.

On the other hand, the body has two sources of water-supply—the water taken in as such and the water content of the ingested food; furthermore, it has been estimated that on an average mixed diet, such as has been referred to, about 12 c.c. of oxidation water is produced for each 100 calories. This oxidation water results from the oxidation of the hydrogen of the carbohydrates, fats, and proteins in the intermediary metabolism. Despite the obviously enormous variations which must exist, a desirable average water intake may be put down perhaps as between 1 and 2 liters per day. Even wide digressions from this figure in either direction, however, are readily compensated for by

one or other means and without apparently harmful results, although any long-continued low intake would in all likelihood lead to more or less renal irritation as a result of continued secretion of concentrated urine. Excessive fluid intake is commonly compensated for by polyuria and diarrhea without obvious deleterious results.

Proteins.—Much that has been said about total caloric value applies with equal force to the protein content of the diet. It must not be too low lest starvation occur, nor must it be too high for good but less important reasons. Not only must the total content of protein in a diet be considered but also, and of more importance perhaps, the variety of protein. For it must be remembered that it is by protein that bodily repair is carried on, and that for this repair or replacement certain combinations of protein-forming amino-acids are necessary. In many proteins one or more important amino-acids are lacking, or are present in very small and insufficient percentages, and these proteins, such as bread, beans, and indian corn, are, therefore, considered as inferior proteins. On the other hand, superior proteins are those in which the constituent amino-acids are those required for the construction of the proteins of the human body. The superior proteins, as might be anticipated, are those of meat, fish, milk, and eggs. For example, the protein of milk casein is capable of supplying all the amino-acids necessary for the formation of even the most complex proteins of the body, and so casein is a complete food and can cause normal growth. Human life can be supported on a combination of inferior or vegetable proteins, and cattle do exist on such a diet, but to supply with this diet sufficient quantities of those essential amino-acids which are present in vegetable proteins in such small amounts demands a very excessive intake, and brings us back to the same questions as we discussed under vegetarianism.

Many of the feeding experiments planned to demonstrate the insufficiency of individual vegetable or grain proteins to produce growth have been interfered with by our lack of detailed knowledge of the so-called vitamins or accessory dietary substances, which will be discussed later. But much has been learned by such

experiments, and today the individual deficiencies of some of the vegetable proteins are known, and may be corrected by the addition of proteins containing the missing amino-acid units, with resulting successful growth.

The amino-acid which in any protein is present in so small an amount as to limit the biologic value of the protein has been spoken of as the limiting factor or limiting amino-acid. A short time ago it was believed that the failure of many single proteins to act as sufficient sources of all amino-acids to produce growth could be explainable by a deficiency in some one limiting amino-acid, but it is now claimed that the proof of this is lacking, and that in many instances no one amino-acid is the limiting factor.

Theoretically, an adult should exist in protein balance or equilibrium, neither losing nor retaining nitrogen, and, as it has been shown that about 20 per cent. of the weight of an average man consists of protein, and that the daily irreducible minimum of wear and tear is about 2.5 parts per 1000, it can be seen that the lowest sufficient protein diet must be one which will replace this loss. The amounts of various proteins necessary to thus protect the body from protein loss have been shown to be as follows: Meat protein, 30 grams; milk protein, 31 grams; rice protein, 34 grams; potato protein, 38 grams. It has, therefore, been generally accepted that the minimal protein intake that will maintain nitrogen equilibrium is never below 30 grams and varies up to 80 grams a day. An average individual on a mixed diet, and taking no thought of the protein intake, is said to consume from 56 to 84 grams of protein per day, which amount will adequately protect against protein loss and its serious results.

Superfluous protein in moderate degree is far from being harmful and, in fact, is beneficial. The excess is oxidized and supplies heat and energy to the body, and such a moderate excess of valuable building materials and fuel may be considered in the nature of a factor of safety (Meltzer).

If an average diet contains 100 grams of protein there is seldom danger of protein deficiency, and the usual error is in the other direction. All proteins are broken down, but the excess amino-

acids undergo deamination with the formation of ammonia and urea, which must be eliminated by the kidneys. Here is one point at which an excessive protein diet may produce trouble. The nephritis so often seen in old diabetics may well be due, at least in part, to the enormous excess of proteins often habitually taken by such individuals in the attempt to satisfy their craving for food without overstepping their carbohydrate ration. Sometimes the ultimate results are worse than if the patient had been allowed to continue with a slight glycosuria. Another possible result of excessive protein intake lies in the failure of the intestinal tract to be able to digest all of the protein. If not digested, decomposition occurs, and, although proteins are not as liable to undergo decomposition as sugars, yet the products of protein decomposition are said by some to be most injurious in the production of that much mooted syndrome—auto-intoxication. We may, therefore, summarize that 100 grams is a satisfactory average protein intake, that 40 grams is a minimum which is lowered only at a risk of protein starvation, and, third, that a maximum cannot be stated, but it is claimed that the Eskimo averages 282 grams without bad results. If bad results should follow the excessive use of proteins they would probably be seen in the development of nephritis, auto-intoxication, or gout, which will be more fully discussed later.

Fats.—Here we approach very unsettled ground. Since the part played by fats in our bodily metabolism is almost wholly as fuel, and since large amounts of fats can be stored in our body, it becomes almost impossible to state the necessary or desirable limits of dietary intake. However, it must be remembered that fat has a value as a fuel food more than twice as great as carbohydrate, and it is difficult to supply a proper caloric diet without introducing some fat, perhaps up to the amount of 50 grams given in our average diet. This amount, which is a very small part of the bulk of the total diet, supplies about one-sixth of the caloric value, and it would require considerable carbohydrate to replace it. On the other hand, the human intestine cannot absorb more than about 300 grams of fat in twenty-four hours, and so our upper limit of intake should certainly not be over 330

grams, which allows for 10 per cent. of non-absorption. The results of too low fat diet may not be serious if an otherwise sufficient diet be taken, but excessive fat ingestion will soon lead to obesity, and will frequently result in severe diarrhea, with the passage in the stools of considerable quantities of unabsorbed fats. In addition to obesity developing in a normal person from excessive fat intake, an accumulation of fat may develop on a much lower diet if the combustive powers of the body are subnormal. This latter has been called "endogenous" obesity in contrast to the former, or "exogenous," obesity. The obesity seen in certain disturbances of the endocrine glands is of the endogenous variety. The evil results of obesity need not be considered here except to mention myocardial insufficiency, poor resistance to infections, and tendency to diabetes. In this latter connection the catabolism of fats must be remembered, and the fact that the fat of the body is derived not only from ingested fats but also from the protein and carbohydrate. The fat ingested undergoes cleavage into soaps and glycerin, and after absorption is resynthetized into the peculiar fats of the body. During the normal intermediary metabolism of fats the fatty acid chains are catabolized, and the ketonic acids, beta-oxybutyric and its lower products, diacetic acid and acetone, are formed. Normally these are intermediary products and are promptly further catabolized and do not appear in the urine. In diabetes, however, these intermediary products are not further broken down, but accumulate in the blood, and are in part secreted by the kidneys. Under such conditions an excessive fat diet may lead to serious results by increasing an acidosis, but there is no evidence to show any such effect from excessive fat ingestion in a non-diabetic individual.

Finally, it matters little, as might be anticipated from what we know of fat metabolism, what variety of fat is taken, for they are all utilized in the production of the three glycerids found in all animal fats—tripalmitin, tristearin, and triolein.

Carbohydrates.—In the average normal diet previously referred to the amount of carbohydrate is put down as 400 grams. This amount of carbohydrate supplies three-fifths of the total cal-

ories, and the foods which contain it constitute about two-thirds of the weight of the whole diet. Of course this latter figure varies enormously with the form in which the carbohydrate is taken, for the content of carbohydrate in food varies all the way from the 100 per cent. in simple cane-sugar to the merest traces of available starch in some of the green vegetables. In fact, many of the green vegetables owe their value as food more to their content of mineral salts and chlorophyl than to the small amounts of carbohydrate in them, and, indeed, it is doubtful whether this small amount of carbohydrate, which to a great extent is in the form of cellulose, is available at all. We must, therefore, always remember that it is the actual available carbohydrate content which must be reckoned on, and not the total bulk of carbohydrate-containing foods.

Since carbohydrate is of value chiefly as a fuel food, a reduction in the amount ingested is not of serious import unless it results in an undue increase of the other two dietary constituents. Furthermore, the body's need for glycogen can be supplied from the sugar formed in the metabolism of the protein and fat of the food or of the body itself. Thus, a diet low in carbohydrates may be a sufficient diet, but it will usually be either low in total calories or too high in protein or fat. On the other hand, an excess of carbohydrates may produce ill-results which depend somewhat upon the form in which the carbohydrate is eaten. The carbohydrates which are taken as disaccharids and polysaccharids must be broken down during salivary and intestinal digestion to the simpler monosaccharid form before absorption can take place. The monosaccharids derived, for example, from starch, as well as the monosaccharid sugars ingested, are absorbed directly and pass to the liver by the portal circulation.

In the liver glycogen is formed synthetically and stored in the liver and muscles. If the amount of sugar in the blood is in excess of the ability of the liver to form glycogen, hyperglycemia develops and some of the excess is passed off by the kidneys. Glycosuria thus caused is called alimentary glycosuria, and, theoretically, this limit of tolerance should determine the upper limit of carbohydrate ingestion. Practically, however, alimentary glycosuria

does not follow even excessive ingestion of starches in the normal, since the breaking down of this polysaccharid takes time, and the monosaccharids are, therefore, only gradually available, and are never presented so rapidly to the liver as to exceed this organ's glycogen-forming ability. In addition, there is usually a limit to the power of the intestinal tract to absorb sugars, and this factor helps to protect the liver from too rapid a flooding with sugar. On the other hand, if sugar beyond a certain amount is absorbed the liver is overwhelmed and alimentary glycosuria appears. Similarly it has been shown that glucose may be introduced intravenously in men over a number of hours without the appearance of diuresis or glycosuria if the rate of introduction be kept below 0.85 gm. per kilo per hour. Even a normal adult will usually show a glycosuria after the ingestion on an empty stomach of 100 to 200 grams of glucose dissolved in water or tea, but in many instances a much higher tolerance is found in normal individuals. A diminished tolerance, of course, suggests a diabetic tendency, while an increased tolerance is described in certain cases of hypopituitarism.

Here at the University Hosiptal we have had referred to us several cases with a diagnosis of diabetes mellitus which, on study, turned out to be instances merely of this alimentary glycosuria. One case was of considerable interest—the patient was a young woman of twenty-five years who was admitted complaining of thirst and loss of weight. Her complaints dated back eleven months, and about three months before admission sugar had been discovered in her urine. Throughout her illness she had noticed that she was more than usually fond of candy, pie, cake, and ice cream. In her family history diabetes is reported only once, in a distant cousin. The patient was working in a candy factory.

Her physical examination was negative in all respects. Her urine, collected for the first twenty-four hours in the hospital and while on a general diet, was found to contain 8.5 per cent. of sugar or 183 grams to the whole specimen. No acetone or diacetic acid was present. The patient was then placed upon a carbohydrate-free diet, and sugar was not found in the first twenty-four-

hour collection on this diet, and at no time did it reappear while this diet was continued. Within a few days after becoming sugar free she was able to take 50 grams of glucose on an empty stomach, with the appearance of mere traces of sugar in the urine. At times she showed traces of acetone, and once diacetic, and she finally left the hospital sugar free on a diet containing moderate amounts of carbohydrates.

In view of such cases, it seemed that it might be of interest to examine the urine of persons working under conditions apt to lead to excessive sugar intake. Through one of the hospital social service workers the urine of ten candy-shop salesgirls were obtained, and it was found that one showed a constant slight glycosuria. Upon inquiry, it was found that this girl was known in the store as a "nibbler," and was the only one of the ten who did eat much candy. This girl was brought to the hospital and her blood-sugar determined, but no hyperglycemia was demonstrable, and she was apparently in perfect health. No opportunity to perform an alimentary sugar-tolerance test was obtained and she has since been lost sight of.

Such a state of affairs cannot be uncommon, and has its chief interest in the possible influence of such a continued excessive carbohydrate intake on the later development of a true diabetes. Diabetes is certainly more common in "good livers," and the not uncommon occurrence of conjugal diabetes suggests the possible influence of dietetic habits. Theoretically, a long-continued overstrain on the organs concerned in carbohydrate metabolism the result of an excessive use of carbohydrate might, in certain instances where there is a weakness of this function, eventually lead to a breakdown of the mechanism and the development of diabetes.

Thus we see that even considerable variations in the part played by sugar and starches in our diet are followed by no immediate or direct ill-results.

Mineral Salts.—A mixed diet contains inorganic constituents, both in organic combinations and as soluble and insoluble salts. The mineral salts exist in nearly all our foods in a total percentage of about 1 per cent., but there is a great variation in

the quantitative occurrence of each salt in different foods. On the whole, however, almost any diet satisfactory in other respects will fully supply all the body's mineral needs. It has been claimed that an average total excretion of mineral matter per day in the urine, feces, and sweat is in the neighborhood of from 20 to 25 grams, and since our bodies tend to maintain a balance between mineral intake and out, it follows that the above amount must approximate the mineral content of an average diet. Not only does the body maintain an equilibrium between the total output and intake but also for each individual element under very different conditions, however. Iron metabolism will well exemplify this.

Iron to form hemoglobin may be obtained by the body either from the hemoglobin of ingested meat or formed from vegetable chlorophyl. Almost any diet will supply us with iron in great excess to our needs, for, owing to the very slight daily loss of iron, the body needs but very little, and anemia from lack of iron in the diet is seldom if ever seen. A marked exception to this general rule is milk, which, while in other ways an almost perfect food, is lacking in its iron content. In infancy this lack is balanced by a great storage of iron in the liver and spleen of the newborn child. Incidentally, the elimination of iron is almost wholly through the bowel, only minimal amounts being found in the urine.

Calcium metabolism is still too little known for us to draw any sure deductions concerning the importance of calcium in the diet. Rickets has been attributed by some to an insufficiency in dietary calcium, and a greatly increased excretion of calcium is seen in tetany, but no relationship to the diet has been proved. With regard to calcium and also phosphorus it must be remembered that the bones contain enormous stores of these substances which can be drawn upon by the body to some extent in times of need.

Sodium Chlorid.—More important from a dietary point of view than the other inorganic elements is sodium chlorid. It is important not only because it is essential to bodily health and is harmful in excess but also because with our present dietary habit of using salt as a flavoring it is not uncommon for harmful

variations in our salt ingestion to occur. Table salt usually contains from 97 to 99 per cent. of sodium chlorid, and our free use of this flavoring not only at the table but also in cooking makes the smaller amounts normally present in many foods almost neglible in the supplying of our needs. Meat eaters can dispense with added salt, but vegetarians cannot, not only because vegetables contain too little sodium chlorid but also because vegetables contain considerable potassium, which must be balanced in the body by sodium.

It is said that the average consumption of common salt is about 19 grams per day, exclusive of the small amounts originally present in the food. Normally the output of salt in the urine and sweat closely follows the intake, and if the intake is much reduced, the output rapidly decreases. During fasting the sodium chlorid output sinks well below ½ gram, while the potassium excretion, which is normally much lower than the sodium, may become higher, and so approach the normal relationship of these substances in the tissues.

Life can be maintained for a long time on a very low salt intake, but health will always eventually be impaired. Too great a diminution of sodium chlorid intake will lead to anemia and to a lowering or absence of hydrochloric acid in the gastric secretion.

The results of excessive ingestion of salt depend to a considerable extent upon the functional ability of the kidney to excrete salt. If, however, the amount of salt taken in is greater than the kidney can easily dispose of, a tendency to edema appears, and it is probable that there are many cases of slight salt retention. Such retention may be the first evidence of an insidiously developing nephritis, or may be due to the overburdening of a normal kidney. There are individuals who habitually whiten their food with salt, and who obviously must be putting a tremendous strain on the kidneys' function along this line, which may predispose, or even eventually lead, to a nephritis.

There is some evidence that some cases of transitory edema and even angioneurotic edema are related to excessive salt ingestion. We have had in this hospital a case of so-called angio-

neurotic edema whose attacks of edema seemed to be largely controlled, although not entirely prevented, by a reduction in her salt intake. There are other cases in which headaches have been relieved by a low salt diet. It seems probable, therefore, that evil results may follow directly on an excessive intake of salt and that nephritis may be a distant result. How much salt should be considered an excess is impossible to state, as individuals vary, but an ingestion of over 30 grams a day had better be considered as questionable.

Vitamins.—During the past twenty years our knowledge has been greatly increased concerning a group of substances whose absence from a diet bring about serious results. These have been called "vitamins" and also "accessory food substances." Two lines of investigation have given us most of our information on this subject, and both have led to quite similar conclusions. On one side, the studies of the dietary insufficiencies in growth experiments proved that it was impossible to nourish animals on diets composed of purified proteins, fats, and carbohydrates, and later experiments showed that this was in most instances due to the removal in the process of purification of some unknown substances. On the other hand, it was demonstrated that a polyneuritis analogous to human beriberi could be produced in fowls by restricting them to a diet of polished rice, and that rice from which the covering cortex had not been removed by polishing would relieve the symptoms. These substances, which were lacking in purified diets and in polished rice, were named "vitamins," and because this name suggests a chemical structure which is as yet unproved some have objected to it and prefer the simple descriptive term "accessory food substances."

Four pathologic conditions have each been attributed by some writers to the lack of a specific accessory substance. These four are beriberi, scurvy, rickets, and pellagra, and, while evidence in beriberi is most conclusive, that presented concerning the other three conditions is far from satisfactory. Other investigators, especially McCollum, claim that there are but two of these accessory food substances, a fat-soluble factor A and a water-soluble B. The former is present in milk, egg-yolk, animal tissues,

vegetable leaves, and to a much smaller extent in seeds. The latter is present in most food-stuffs of vegetable and animal origin, but is almost lacking from "crystalline sugar, starch, and fats, and is present in but small amounts in polished rice and probably in those foods derived from the endosperm of seeds by milling processes." Human beriberi, or the polyneuritis of fowls, results from a diet insufficient in this water-soluble B, and extracts containing this fraction act in a promptly curative manner. The wide occurrence of this unrecognized substance in most foods makes it obvious that the danger of deficiency in this direction is very remote under normal conditions. Similarly, in the cure of experimental neuritis and of beriberi many substances have been found available. Formerly rice polishings were always selected because it was due to their lack that the condition developed, but now it is known that brewers' yeast and the coverings of many grains and legumes also contain sufficient vitamins to supply the deficiency.

As has been said, scurvy, rickets, and pellagra have been attributed, especially by Funk, to deficiencies in specific vitamins. The development of scurvy on shipboard under conditions of very limited diet with no fresh food suggests such an etiology, but McCollum has cured experimental scurvy in guinea-pigs as easily with inert mineral oil as with the accepted antiscorbutics, such as orange-juice or potato. He believes that scurvy in the guinea-pig is the result of the character of feces produced by certain diets, with secondary injury to the bowel wall and resulting infection. It must, however, be remembered that, although scurvy in the guinea-pig seems closely analogous to human scurvy, their identity is not certain, and until further evidence is obtained the subject must be considered unsettled.

The evidence in the case of rickets is as yet very indefinite and need not be discussed. Pellagra, however, does not seem to offer by analogy to beriberi many arguments in favor of its being due to some vitamin deficiency, and if this is so, the deficiency occurs as a result of a diet too limited in meat and fresh vegetables, or because the maize which constitutes so very important a fraction of the diet in the districts in which pellagra

is common is itself deficient or even possibly toxic. There has been some investigation which tends to suggest that pellagra is common in those districts in which the grain is sent to a mill for grinding and not ground at home by hand. The mill-grinding is supposed to remove certain essential elements in the grain just as polishing does in the case of rice. On the other hand, there is much evidence pointing away from this theory, and the question must be considered as unsettled, although the present-day tendency is to believe that a still unrecognized dietary deficiency is an important element in etiology of this disease.

There have been attempts to identify the chemical nature of these so-called vitamins with only partial success, but with very interesting results. Funk's experiments have led to the conclusion that "it is not unlikely that nicotinic acid is a decomposition product of the vitamin," and Williams' work has shown that certain crystalline forms of certain substances, especially α-hydroxy pyridin, have strongly curative powers for dietetic polyneuritis in pigeons. Williams points out that nicotinic acid and the substances with which he worked are similar in being closely related to a betain, and that a "feature, conforming more or less closely in structure or energy conditions to the type of the betain ring, is probably an essential characteristic of antineuritic vitamins." There are other theories, and we must await further facts.

As to the amount of vitamin required little is known, but Seidell has estimated that the daily vitamin requirement of a grown pigeon is less than 1 mg., which is about 0.0033 per cent. of the bird's diet. Perhaps a similar percentage will suffice in man. At any rate, it is certain that any reasonable diet will contain a sufficient quantity of each, and so under normal conditions they do not influence us in our choice of foods, but it is evident that they form an essential bodily need, and that under abnormal food conditions they may play a most important rôle. Quantitatively we know nothing, but qualitatively it is obvious that to avoid ill-results we are forced to avoid a diet too purified or too limited in meats and fresh or undecorticated grains.

There is no evidence that an excess of such accessory food substances is in any way harmful, but it is probable that there is

much to be learned concerning these vitamins, and that to the small number of pathologic conditions which we now recognize or suspect as being due to a deficiency in these substances others will be added possibly due not so much to an actual deficiency as to a lack of balance.

In fact, in all dietary problems there are two most important considerations which we can afford to ignore. One is balance and the other palatability. The psychic influence on digestion is constantly in evidence and must be catered to. Balance is essential. A marked variation in one factor in one direction will cause a contrary variation in other factors and the diet will cease to be satisfactory.

We see, therefore, that although nature permits us quite wide variations in respect to our total diet and to its individual constituents, yet beyond these limits there are quite rigid boundaries which we cannot cross for any period without disturbance and ultimate injury.

So long as we remain within these limits we are protected and guaranteed a considerable factor of safety against unusual stress and demand. In health this may not appear to be of great importance. In disease, however, the limits within which we may vary the diet are greatly narrowed in one direction or another, and the proper diet in any disease is one which is restricted within the narrowed limits peculiar to that disease. Such a diet can only be properly constructed by one in full knowledge not only of the normal, but of the pathology and altered metabolism of the disease at hand.

CLINIC OF DR. JAY FRANK SCHAMBERG

POLYCLINIC HOSPITAL

THE CAUSES OF REACTION AFTER SALVARSAN[1]

THE employment of salvarsan in syphilis with the idea of effecting a rapid sterilization by destroying the spirochetes at a single or by several repeated strokes was a new conception in drug therapy. Rapid cures can often be accomplished in primary syphilis and pretty constantly in yaws—a tropical disease closely related to but feebler than syphilis—but experience has proved that the early hopes of Ehrlich of a therapia sterilisans magna have not been realized with regard to the disease generally. Salvarsan has a remarkable affinity for spirochetes and trypanosomes, and has a relatively low affinity for the body cells. No one could contend, however, that it is devoid of organotropism. By reason of the fact that it does not combine readily with the protein of the body cells, it can be given in large doses, and it is in part because it can be administered in massive quantities that its effects upon the symptoms of syphilis are so magical. If mercury could be administered in the dose of 600 mg. instead of about 15 mg. it is quite possible similarly remarkable results might be obtained, but mercury is much more of a poison to the tissues than salvarsan, and its intravenous tolerated dose in animals is about fifty times less.

There are various types of reaction that may develop after the administration of salvarsan. Everyone is familiar with the *vasomotor reactions* which not infrequently manifest themselves before the intravenous infusion is completed, or immediately thereafter.

[1] The laboratory results referred to in this communication are based upon the investigations of Dr. John A. Kolmer, Dr. George W. Raiziss, and the writer carried on in the Dermatologic Research Laboratories of the Philadelphia Polyclinic.

The commonest early symptom is flushing of the face, although an earlier symptom with some patients is a peculiar gustatory sensation, often of an ethereal character, the patient remarking that he can taste the drug. A burning sensation of the lips or tongue may be complained of. The flushing may be slight and transitory, or it may be pronounced, accompanied by injection of the conjunctivæ, lacrimation, edema and swelling of the lips, tongue, or eyelids, an anxious expression of the countenance, cyanosis, nausea followed by retching and vomiting, and this, in turn, by profuse perspiration. In some cases cough, respiratory embarrassment, and dyspnea are observed. The pulse at first is full and bounding, but later slow and of very small volume, in which event it is usually accompanied by a death-like pallor. In severe cases the patient may lose consciousness and the pulse may be scarcely palpable at the wrist. In some cases epileptiform convulsions may take place, and patients are known to have fallen off the table from the violence of the convulsive movements. In rare instances death has occurred, although most patients, even when apparently *in extremis*, will recover from the attack. Among uncommon symptoms observed during the stage is an urticarial eruption, and in other patients a severe pain in the lumbar region in the vicinity of the kidneys. The symptoms just described may disappear in fifteen minutes, being followed by considerable lassitude. As a rule, later reactive manifestations of a different character manifest themselves.

Febrile and Gastro-intestinal Reactive Manifestations.—These symptoms usually make their appearance about three hours after intravenous infusion of the salvarsan solution. The patient commonly complains of one or several of the following symptoms: headache, chilliness, or active rigor with shivering, fever, nausea, vomiting, and diarrhea. These occur in varying grades of intensity. The patient may merely feel "queer," or there may be repeated chills, numerous attacks of emesis, and profuse and protracted diarrhea. Occasionally severe pains in the back and limbs are complained of. This complex of symptoms usually subsides in three to six hours and is followed by a feeling of lassitude or weakness. In rarer instances vomiting and

diarrhea, associated with fever, may continue for a number of days, the patient being unable during this time to retain any nourishment. A patient under my care ran a temperature of 104° F. for three days following the administration of salvarsan, but made a good recovery. In some instances the urine may be scanty and contain albumin and casts.

Certain eruptions have been observed to develop at times after the administration of salvarsan, appearing either in a few hours or several days. These have been of an urticarial, scarlatinoid, or morbilliform character. In rare cases the eruption has been purpuric. I have in several instances observed a pruritus or itching of the skin, unaccompanied by any eruption. Most of the eruptions are evanescent and disappear after a few hours' or days' duration. Later more persistent and more serious eruptions have been observed to occur about six to ten days after the administration of salvarsan, more particularly when the drug has been given by the intramuscular route. Some instances of universal exfoliative dermatitis have been reported persisting for weeks, with fever and debility, and sometimes leading to fatal termination.

A third group of *serious late reactions* comprises those which come on one or several days after the administration of the drug and which are characterized by alarming brain symptoms. In some cases there may be headache, vomiting, muscular twitchings, epileptiform convulsions, dilatation of the pupils, absent reflexes, coma, and death. These cases are usually the expression of an *edema of the brain* or an *encephalitis hemorrhagica*. Meirowsky and Kretzmer have shown that of 109 fatalities after salvarsan recorded in literature, 41 per cent. occurred in the secondary period and 29 per cent. in late nerve syphilis. Three-fifths of the fatalities during the secondary period resulted from encephalitis; 45 per cent. of these occurred in cases in which the dose exceeded 0.5 gram. The size of the dose and the frequency of the injections bear a direct relationship to the incidence of encephalitis.

Another rare syndrome following the administration of salvarsan is characterized by severe jaundice accompanied, as a rule,

by fever. This may appear in from three days to several weeks after treatment. Such accidents are much more frequent after intramuscular than after intravenous injections. Most cases of postsalvarsan jaundice pursue a favorable course, but there are exceptional cases which terminate fatally, with the symptoms and autopsy findings of acute yellow atrophy of the liver.

The Causes of Reactions.—It might be pertinently asked whether these various groups of symptoms are due to one and the same cause. I may say without fear of contradiction that they are not. A large number of factors have been invoked by an equally large number of writers and clinicians to explain the cause or causes of the reactive phenomena following the administration of salvarsan. Neisser regarded the febrile reactions as due to an endotoxemia caused by massive destruction of the spirochetes and liberation of their products. Luitheln and Mucha believed that the fever, headache, vomiting, etc., were due to a resorption of broken-down cell products. Wassermann advanced the hypothesis that water impurities, chiefly bacterial proteins, were largely responsible for the febrile and gastro-intestinal symptoms. I might enumerate many other theories advanced to explain the cause of reactions, but without profit to the reader.

The principal fact to be emphasized is that a variety of factors may be responsible for the production of reactive phenomena, but that some are relatively unimportant as compared with others.

These various factors may relate (*a*) to the individual, (*b*) to the technic of administration, and (*c*) to the drug employed. There can be no doubt that individual susceptibility plays a part in reactions. Patients suffering from syphilis vary greatly in their physical condition and in the degree of functional and organic integrity of the various organs. As a class, too, they are prone to be neurasthenic, and the mental state at the time of injection doubtless influences the incidence of some of the less severe reactive phenomena. Patients may vary in their psychic response to the operation, *per se*, in the manner in which they react to errors of technic, and in their susceptibility to the drug itself. Two individuals may receive a solution of the same drug

prepared at the same time, and one may suffer reaction and the other remain free. The writer had a striking example of this in his practice. A physician and his patient each received half of the quantity of an alkaline solution of salvarsan from the same mixing cylinder. The physician shortly afterward developed pronounced chills, elevation of temperature to 102° F., and severe pains in the legs; the other patient, contrary to instructions, ate a hearty meal an hour later and took a two hours' train ride to a neighboring city, but suffered no reaction. There can be no doubt, therefore, that the personal element may be a factor in causing or influencing reactive symptoms, but it is, in my opinion, not the dominant factor.

Various imperfections in technic may give rise to febrile and gastro-intestinal reactions. I recall a patient in whom unsterilized water was, by inadvertence, used, with the induction of fever, severe diarrhea, and debility lasting for over a week. Febrile and gastro-intestinal symptoms may result from the use of imperfect water, but all such reactions are not, of necessity, due to this cause.

Failure to neutralize the salvarsan solution may give rise to severe reactions in which several rather characteristic symptoms are present; in these cases the patient complains of severe pain in the chest and cough, coming on rather quickly and persisting for a number of days. Cyanosis may also be present. Nausea, vomiting, and other symptoms may be present. The chest symptoms are due to precipitation of the acid salvarsan in the capillaries of the lungs. I have known of several cases where physicians, from carelessness or other cause, failed to neutralize. Two patients with severe reactions recovered and one died. Several other physicians have written to me that they have given the acid solution without bad after-effects. Much, of course, depends upon the concentration of the solution. The precipitate formed in the capillaries is in direct relation to the degree of concentration. Acid solutions are 50 to 60 per cent. more toxic than the neutralized solution, and in concentrated solutions the toxicity is still further increased.

There are other faults of technic which may likewise be re-

sponsible for reactions, such as the use of too hot or too cold water, too alkaline solutions, the employment of too small or too great a volume of water, the too rapid infusion of the solution, etc. Then, too, the improper preparation of the patient for the injection or improper after-treatment. The intravenous administration of the drug shortly after the eating of a meal or the partaking of food too soon after the injection may induce gastro-intestinal reactions. Physical overexertion immediately before or directly after treatment may likewise be responsible for reactive phenomena.

Dr. George A. Raiziss, Dr. John A. Kolmer, and myself have been particularly interested in the question of the relation of the drug itself to reactions. We are convinced that variations in the drug with the consequent development of traces of impurities are more responsible for reactions than any other factor.

At the outset it must be recognized that salvarsan is an extremely complex compound, the most difficult to prepare of any drug employed in medicine. Almost a score of chemicals and almost four score of operations are necessary before its final elaboration. There are opportunities for the development of traces of impurities in the finished product, inasmuch as the latter cannot be repurified by repeated crystallization. It is due the medical profession to state that salvarsan of absolute chemical purity does not exist. It invariably contains certain impurities. My colleagues and myself are convinced that *the early vasomotor symptoms are due to an impurity in salvarsan.* We have devoted much study to a search for the particular chemical variation which gives rise to these phenomena, but thus far our efforts have not been attended with success. We feel justified in stating, however, that the symptoms are due to an unidentified impurity which, for purposes of reference, we have termed substance X.

Substance X has a powerful vasoparetic influence. It induces dilation of the blood-vessels, followed in many instances by leakage of serum into the tissues. It is this serous exudation which gives rise to puffing of the eyelids or lips which is at times

observed. The paretic influence upon the vessels may be so severe in some cases as to lead to collapse of the patient. Whether the presence of substance X could play a part in the production of edema of the brain or encephalitis hemorrhagica in the cases in which these rare complications develop, is rather doubtful, in view of the fact that these symptoms usually come on late—*i. e.*, twenty-four to seventy-two hours after the drug is administered.

The question might be asked, Why are the vasomotor reactions attributed to an impurity in the drug? We have found that certain serial lots or batches of the drug give rise to no flushing or vasomotor phenomena whatsoever, whereas certain other lots give a high incidence of such reactions. I am administering at the present time ampules from a certain lot of arsenobenzol, which permit of the full 0.6 dose being given almost indiscriminately to patients without any flushing or other vasomotor phenomena, and with a very small percentage of febrile and gastro-intestinal reactions. On the other hand, we have had one particular batch of arsenobenzol which gave quite a high percentage of vasomotor reactions. There is no other explanation of the cause of these reactions than some ingredient in the drug. Unfortunately, it has thus far been impossible to detect the difference in the compounds by ultimate chemical analyses. Furthermore, the animal toxicity tests do not always disclose the presence of substance X. Animals survive or die, but do not exhibit any reactive phenomena such as are observed in man. Fortunately, the method which we employ in our laboratories lessens to a marked degree the formation of substance X in salvarsan. We shall continue our investigations with the hope of isolating and identifying substance X, and thus consistently eliminating it from the compound. The late severe hepatic degenerations which have occurred in rare instances may be due, as Ehrlich suggests, to a splitting off and oxidation of the arsenical group. The febrile and gastro-intestinal reactions may be due to a considerable variety of causative factors; the early vasomotor symptoms are due chiefly if not exclusively to the drug.

The problem of preparing a salvarsan as chemically pure as possible, and one that can be given with little or no reaction, is of importance, because such a compound could be more intensively administered—*i. e.*, in full dose and at shorter intervals than usual—and thus a more profound and more curative impression made upon the disease.

CLINIC OF DR. ELMER H. FUNK

JEFFERSON HOSPITAL

OSTEITIS DEFORMANS

Report of an Early Case

First Described by Sir James Paget in 1876. Number of Authentic Cases Recorded to June 1, 1917. Frequency of Occurrence. The Typical Appearance of Advanced Stages of the Disease. Picture of Such a Patient. Case Report of Patient in the Early Stage with Single Bone Involvement. x-Ray Findings. Discussion of the So-called Mono-osteitic Types. Symptomatology—Onset, Pain, Deformity, etc. The Supervention of Malignant Disease and the Relation of the Tumor-forming Osteitis Deformans of von Recklinghausen. Etiology. Metabolic Studies. The Metabolic Picture to a Certain Degree the Reverse of Osteomalacia. Treatment and Prognosis.

FORTY-ONE years ago Sir James Paget presented before the Medico-Chirurgical Society of London a paper on a rare form of chronic inflammation of bones, with a report of 5 cases. He called the condition osteitis deformans, and since his time there have been reported approximately 232 authentic instances of the disease. In its advanced stages the appearance of the patient is typical, and several writers have noted that a comparison of the photographs of reported cases suggests a family similarity. I want to pass around to you a picture of a well-developed case which came under our observation several years ago, and which was reported by Dr. J. Chalmers DaCosta and me. You will note that the patient presents an unmistakable clinical appearance, so that once seen, it is scarcely possible other cases would go unrecognized. Its rarity is evidenced by the fact that only 3 cases occurred among 38,000 admissions to the New Jefferson Hospital during a period of seven years. A similar incidence was noted by Hurwitz, who found only

3 cases among 30,000 medical admissions to the Johns Hopkins Hospital.

The patient which I want to bring before you today repre-

Fig. 39.

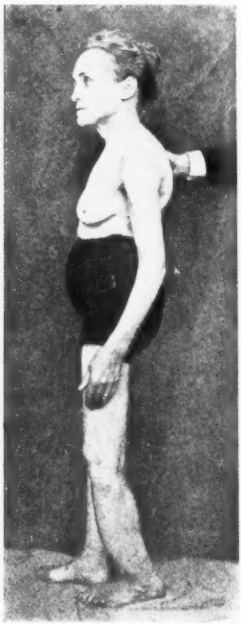

Fig. 40.

Fig. 39.—Case showing advanced disease. Note the enlargement of the head. The face, which is often described as roughly triangular with base upward (because of greater involvement of cranial bones than of facial bones of skull), is not apparent in the patient because of involvement of lower jaw. Note the thickening of the clavicle, the increase in width of hips, the bowing of the legs due particularly to bending of tibia and fibula on left side and femur on right side. The patient decreased about 7 inches in height. (Osler refers to a case in which the decrease in height amounted to 13 inches.) The arms appear disproportionately long—suggesting a similarity to those of anthropoid apes. The joints are freely movable.

Fig. 40.—Case showing advanced disease. Note the projection of the head, the cervicodorsal kyphosis and marked deformity of left tibia, the site of initial involvement. The difficulties of station and gait are evident from this and preceding picture of patient.

sents an early stage of the disease in which the involvement clinically is apparently limited to one bone, although the *x*-ray examination shows beginning changes in several others.

CASE HISTORY

M. F., female, white, aged fifty-seven years.

Family History.—Negative. One brother and two sisters, one of whom is the twin of patient, are living and well. No one in near or distant family has any condition of the bones comparable to the patient.

Fig. 41.—Patient reported in this clinic.

Past Personal History.—Birth normal. None of childhood diseases. Always been healthy except for an attack of erysipelas when twenty-nine years old which followed incision of a stye on left lower lid. Menses began at fourteen years and stopped at forty-two years. She was married at twenty-two years. Shortly after marriage she had a miscarriage, and the children of two subsequent pregnancies died within one month of delivery. The last two children were born healthy and are now well and robust at twenty-one and twenty-five years of age. Following the birth of the last child she was operated upon for "falling of the womb," following which she made a prompt recovery.

Present Trouble.—About four years ago while lifting furniture in housework she was seized with a sudden pain across the lower back, for which she was compelled to go to bed for one week. She recovered from this, and a short time afterward began to have vague pains, thought to be rheumatic, in upper part of right leg. About the same time, or perhaps a little while after-

ward, she noted that the thigh was bending, and her husband called attention to a limp in her gait. Since the onset the pain, though present from time to time, has become less and less severe and the deformity more and more marked. Quite early she noticed a shortness in the leg which has been increasing until now, when "it is about 4 inches shorter than the other." She states that she is considerably smaller in stature than when she was married, but doesn't know how much. She considers herself in good health except for the inconvenience caused by her deformity. The appetite is good, bowels regular, and sleep normal. She has not noted any alteration in the shape of her head and has never had any headache.

Physical Examination.—Patient measures 4 feet $7\frac{1}{4}$ inches and weighs $116\frac{3}{4}$ pounds. There is a distinct limp to the gait. The *head* seems to be slightly enlarged, though one cannot say so with certainty. It is uniform in contour and the bones of the face are normal. The eyes, ears, and nose are negative. The tongue is slightly coated, and all the teeth have been removed except three upon right lower jaw. The thyroid gland is not palpably enlarged. The *spine* shows a lateral curvature, which is probably compensatory to the pelvic inclination caused by the shortened right leg. There is also a moderate degree of cervicodorsal kyphosis. The *chest* is slightly rounded. The clavicles and bones entering into the shoulder-girdle are not palpably enlarged. The breasts are pendulous, and upon the right side a hard mass is palpable, though freely movable with the breast (on close inquiry, patient states that she has had this lump for ten years, and it has not caused her any annoyance, although she believes it has been distinctly enlarging of late). The skin overlying the mass presents some dimpling. No palpable enlargement of the axillary glands can be found. The lesion is evidently of malignant disease, for which she has been referred to the surgeon. The examination of the *lungs* and *heart* reveals nothing of note. The *abdomen* is short and prominent. The walls are relaxed and protrude in the lower half, suggesting considerable enteroptosis. The liver extends 1 inch below costal margin in right midclavicular line. Spleen and kidneys are not palpable.

The Extremities.—The right femur shows marked thickening throughout its entire course and a marked outward curvature. The hip-joint and knee-joint upon this side move freely and are apparently uninvolved. The remaining bones of the extremities are normal except the lower third of the left tibia, which presents a slight thickening, the result, in all likelihood, of a fracture which occurred at this place three years ago. The reflexes present no alterations. The leg measurements on the two sides are as follows: Anterior superior spine to internal malleolus—right, 27½ inches; left, 30 inches; anterior superior spine to external malleolus—right, 29 inches; left, 29¼ inches.

The *blood* examination revealed Hb. 85 per cent.—reds, 5,020,000; whites, 10,600; differential white count—large mononuclears, 8 per cent.; small mononuclears, 48 per cent.; polynuclears, 38 per cent.; eosinophils, 2 per cent.; transitional, 4 per cent. No morphologic or staining alterations of the red cells. The *Wassermann test* was negative. The *urine* examination was normal.

The *radiographic study* was made by Dr. W. F. Manges, who made plates of the various bones of the trunk and extremities and of the skull. The right femur shows the principal involvement, an extensive bowing outward. The left femur is straight. The right femur shows the characteristic bone changes of osteitis deformans. The bowing of this femur is out of proportion to the increase in diameter. The bone production is in excess of bone absorption, relatively speaking. This gives the bone an unusual density. It is difficult to understand how so great a deformity could have resulted in this leg unless there was a definite stage of softening followed by deformity, and then a stage of increased bone deposit causing this marked density. The great trochanter and the neck of the femur have the more spongy appearance that is characteristic of the disease. There is entire lack of bone detail in the pelvic bones around the acetabulum on both sides. This leads me to believe that the pelvic bones are involved. The skull shows very early involvement. There is a granular appearance in the posterior parietal region which I am unable

to explain in any other way. The skull is, however, not appreciably thickened.

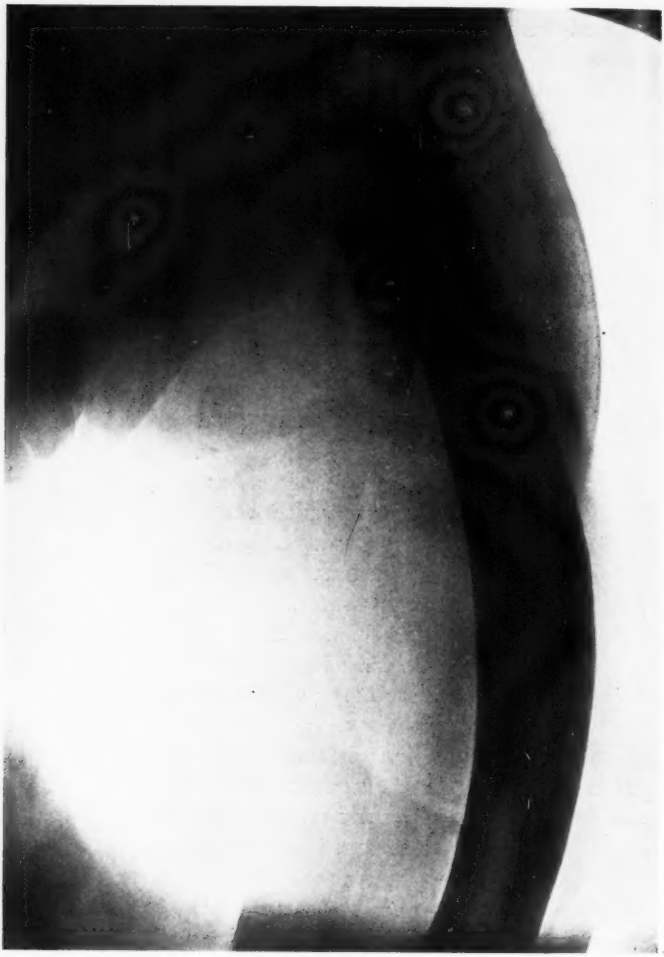

Fig. 42.—Right femur.

This case must have been at some time of the mono-osteitic

type; I cannot be positive that other bones are not involved at

Fig. 43.—Left femur.

present, but they certainly are not involved in proportion to

the condition of the right femur. I believe that this case should be re-examined at intervals in the future, so that we can determine whether or not it is progressive, and perhaps estimate more easily than it is possible clinically the order and rate of involvement.

DISCUSSION

This case is of interest because it represents an instance of osteitis deformans limited to a single bone. I say apparently, because, although one finds clinically no change in the other bones, the *x*-ray examination reveals early changes in the skull and pelvic bones. Paget and the early writers believed in the constancy of multiple bone involvement, but recent observations would seem to indicate that the lesion may be limited to one bone, or at least may be recognized in the early stage before multiple bone involvement has occurred. Schirmer, Bowlby, Schlesinger, Hurwitz, and others refer to cases of single bone involvement. Schlesinger applies the term "mono-osteitic" to this form of Paget's disease. Our case together with those of Bowlby and Hurwitz are the only ones on record in which the disease is limited to the femur, and, strange to relate, the right femur in each case. Just how long the disease may remain localized in a given bone is a matter of conjecture. In Hurwitz's case and in our own four years have elapsed since the patient first noticed the deformity.

The involvement of a single bone is of particular interest with regard to those cases in which gradual enlargement of the skull is the first noticeable feature. Many of these cases of early head involvement have been considered as examples of leontiasis ossea, or Virchow's disease. In the case described by Edes in 1896 the enlargement of the head alone suggested this condition. Subsequently, however, in 1902, the typical multiple bone involvement of osteitis deformans developed. In the first case reported by Elsner asymmetric hyperostosis of the skull preceded by many years the involvement of the other bones. Max Koch demonstrated a case of leontiasis before the German Pathological Society, and showed that the microscopic picture

was similar to that occurring in Paget's disease, and considered the two conditions identical.

Symptomatology.—The *onset* of the disease is usually insidious, and in its early stages presents considerable difficulty in diagnosis. We will consider first the clinical manifestations in the early stages and then in the advanced stages of the disease.

The onset varies in character, and cases may be separated into three groups: First, those in which subjective phenomena only are present. The patient complains of vague pains usually in the extremities or back, and variously described as aching, neuralgic, or rheumatic in character. There is no evidence of bone deformity. In the second group of cases objective phenomena only mark the onset. There is a local bone deformity, usually a thickening and curvature of the tibia, or perhaps an enlargement of the skull, to which attention is called by an increase in the size of the hat. The patient experiences no pain or inconvenience, and frequently fails to consult the physician until the disability of the multiple bone involvement and associated manifestations of the advanced stage of the disease appear. In the third group of cases subjective and objective phenomena mark the onset, and the patient appears complaining both of the vague pains described above with a curvature of one of the bones, usually of the lower extremity. Occasionally, as in the present case, the patient dates the onset to some strain or injury, but a traumatic origin is doubtful.

Pain.—The pain, as stated, is variously described as aching, neuralgic, or rheumatic in character, is frequently paroxysmal, and in some instances nocturnal in accentuation. As a rule, it is not constant, nor does it continue throughout the course of the disease. It may be the earliest evidence of the disease; or may occur coincidently with the appearance of the deformity; or, as in one of our cases, it may not appear until the disease has considerably advanced, and in still other instances it may be absent during the entire course of the disease.

A striking contrast in this respect is presented in the cases reported by J. C. Wilson and R. M. White. Wilson's case, which was reported from this hospital in 1902, was a man sixty-

three years of age, who had first noticed outward bowing of the legs sixteen years prior to his coming under observation. He presented the typical multiple bone involvement of Paget's disease, but at no time during its progress was the deformity accompanied by pain. White's patient, a man fifty-six years of age, had first noticed sixteen years prior to coming under observation a sudden pain in the left hip. From that time he had never really been free from pain, especially during the last ten years. At one time, nine years ago, he was confined to bed for one month because of the pain in his legs. The pain was so severe that he frequently was unable to sleep and was compelled to get out of bed and walk around the room. It was ten years after the onset that he first noticed an enlargement of the right leg just below the knee, which was followed several years later by a similar condition of the left leg. Headache, mostly frontal, but occasionally occipital, was present. When pain is present it is usually referred to the back and lower extremities. It is particularly interesting to note the rarity of pain in the head even in those cases of marked thickening of the skull, as in one of our early cases. In Watson's patient the head enlarged $3\frac{1}{16}$ inches in circumference, requiring increase in size of hat from 7 to 8, but at no time had he any pain or discomfort, although for twenty years he had more or less pain in the bending legs. On the other hand, Hann's case is exceptional. The patient, in whom the disease existed twenty-seven years before death, complained during the last nine years of severe and constant headache unrelieved by drugs, and autopsy revealed many flattened bosses projecting from interior side of anterior half of a very thick skull.

Deformity.—The bones most frequently involved are the long bones of the lower extremity, especially the tibia. The earliest pathologic changes may be equally frequent in the long bones of the upper extremity or other bones, but certainly the deformity is most frequently manifest in the lower extremity, probably because of the effect of weight-bearing and subsequent early bending. The deformity at first usually manifests itself in a single bone, and it may be preceded, accompanied, or followed

at varying intervals by pain, described above. In our present patient pain was present at the onset and at intervals afterward, but has become less severe as the deformity has increased.

A number of instances are reported in which gradual enlargement of the skull was the first feature, and if the patient is a man the demand for a larger sized hat may first call attention to the condition. The right clavicle was the bone first involved in Hann's patient. The bones of the hands and feet are rarely involved even in advanced stages of the disease, yet in the case described by Meier the onset was characterized by enlargement of the external malleolus and of the bones of the foot. Meunier and Beclere have described enlargement of the metacarpus, while Klippel and Weil and Pescarolo and Bertolotti have found involvement of the phalanges with the formation of Heberden's nodosities. These observations are rare and exceptional, and yet their knowledge is essential in avoiding possible errors in diagnosis.

The multiple bone involvement of the advanced stage is practically always bilateral and frequently symmetric. An interesting exception has been reported by Klippel and Weil of a patient in whom the disease was apparently limited to the right half of the skeleton. Moreover, the phalanges upon the affected side were involved and showed Heberden's nodosities. The disease was of eleven years' duration, and the question was tersely put by these authors, "Will the patient always remain a 'unipaget,' or will she ultimately develop lesions of a similar character upon the opposite side of the body?" In Pescarolo and Bertolotti's case the individual bones were uniformly involved to a more marked degree upon the left than upon the right side.

The joints are scarcely ever involved in the disease. In advanced cases limitation of motion of the hip, ankle, knee, or elbow may occur because of interference with motion brought about by the thickening and deformity of adjacent bones. The occurrence of fractures is infrequent and probably no more common than in any other disease.

The Supervention of Malignant Disease and the Relation of the Tumor-forming Osteitis Deformans of von Reckling-

hausen.—There exists among 158 reported instances of osteitis deformans 14 cases associated with tumor growth (Gruner, Scrimger, and Foster). To this number these authors have added a very interesting case eventuating in multiple sarcoma formation. In 5 of 8 cases of Paget traced to the end the patients died of sarcoma, 1 case of which developed twenty-two years after the onset of the disease. Whether the association of malignancy in these cases is to be considered as merely coincidental or not, the fact remains that not a few eventuate in sarcoma, and the explanation is probably to be found in the ill-regulated cellular activity which attends the abnormal bone destruction and bone formation.

In this connection mention should be made of the relation of the tumor-forming osteitis deformans (tumor bildenden ostitis deformans) described by von Recklinghausen in 1891. This condition, probably more commonly known as osteitis fibrosa cystica, was considered by him to be closely allied to, though distinct from, Paget's disease. Bockenheimer and Sternberg maintain that both conditions are pathologically identical. Boit is of the opinion that the leontiasis ossea of Virchow (which observers now believe is a form of osteitis deformans) and von Recklinghausen's disease are histologically identical. There are, however, certain clinical differences of note. Pfeiffer, in an extensive review of the literature, collected 49 cases of osteitis fibrosa cystica. He found, with reference to age incidence, that of this number, 6 occurred in first decade, 29 in second decade, 7 in third decade, 4 in fourth decade, and 3 after fourth decade. In other words, approximately 71 per cent. of cases occurred before twentieth year; 83 per cent. before thirtieth year, and 94 per cent. before fortieth year. This age incidence, compared with that of Paget's disease, is striking. The involvement chiefly of the metaphyses of the long bones (Percy); the tendency to spontaneous fracture, which, according to Pfeiffer, occurred in 20 of the 49 collected cases; the more or less definite appearance of cyst formation in the *x*-ray pictures suggest, in conjunction with the above, a process distinct from Paget's disease, or at least a marked variation from the usual

type. Information of the first importance will be obtained when it is possible to make comparative metabolism studies.

Etiology and Treatment.—The treatment of any disease is so intimately connected, as a rule, with the knowledge of its cause, that where the latter is not known, treatment is unsatisfactory. This is particularly true of osteitis deformans. Certain predisposing factors seem to have an influence, such as heredity, age, and sex. Family involvement is estimated in approximately 7 per cent. of the reported cases. The disease usually occurs after forty years of age, although authentic instances of onset in the second decade, and as late as seventy-nine years, have been recorded. Males, as a rule, are thought to be attacked more frequently than females, although our present case and 3 others out of 5 were females. The French clinicians, following Lannelongue and Fournier, have argued the syphilitic origin of Paget's disease, while English and American observers have minimized this etiologic factor. The Wassermann reaction is positive in only one-fifth of the cases. Antisyphilitic treatment has been tried repeatedly, but without avail. It is unlikely that microorganisms of any type play a causative rôle, although several Italian observers isolated an organism, prepared a vaccine, and claimed to have obtained beneficial results. In 2 cases under our observation bacteriologic studies were made of excised portions of the tibia by Dr. A. G. Ellis, with negative results.

In the light of our present knowledge it seems most logical to pursue investigations of metabolism in this disease, particularly from the viewpoint of the relationship between the disorder of bone metabolism and the activities of one or more of the ductless glands. The importance of the ductless glands in bone metabolism has been amply verified. The association of acromegaly and gigantism with disease of the pituitary and the osseous lesions of cretinism are familiar examples. The studies of MacCallum and Voegtlin have demonstrated the importance of the parathyroid and calcium metabolism. If you care to look up the findings with regard to the ductless glands in osteitis deformans you will find a tabulation in the last volume (No. VI) of the Publications of the Jefferson Medical College and Hospital.

The most complete metabolic studies which have been made in osteitis deformans to date are those performed by Bergeim and Hawk in our Laboratory of Physiologic Chemistry. Bergeim and Hawk's investigations revealed a pronounced retention of calcium, magnesium, and phosphorus, and a pronounced loss of sulphur. These findings are interpreted as indicating a stimulated osseous or osteoid formation, accompanying the resorption of the highly sulphurized organic matrix. In advanced osteitis deformans the first step in the new formation of bone or osteoid tissue may be the production of a highly sulphurized organic matrix, which is transformed gradually by a calcification process, which is accompanied by the deposition of calcium, magnesium, and phosphorus in this matrix. In the course of this calcification procedure we may suppose that a certain quota of the sulphur of the matrix is replaced by the other elements mentioned, a process which must entail the retention of calcium, magnesium, and phosphorus and an accompanying increased elimination of sulphur. The metabolic picture of osteitis deformans is, to a certain degree, the reverse of that seen in osteomalacia. Treatment is unsatisfactory, although we are pursuing at the present time certain studies with a view of influencing the calcium metabolism and hoping to inhibit the progress of the disease. The prognosis as regards ultimate cure is hopeless, although as regards life it is often compatible with a fairly active and long career.

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Da Costa, Funk, Bergeim, and Hawk: Publications from the Jefferson Medical College and Hospital, 1915, vi, 1–44. (This article contains an extensive bibliography both with regard to the clinical and metabolism aspects of Paget's disease.) In the present article references given without the source can be traced by consulting this previous publication. In estimating the number of reported cases to June 1, 1917, the Index Medicus was used to that date.